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TABLE OF CONTENTS

		page	Russ. page
1.	The Viscosity of Binary Mixtures Containing Nicotine. IV. S. F. Babak and V.V. Udovenko	2199	2121
2.	The Viscosity of Systems Containing Nicotine. V. S. F. Babak and V.V. Udovenko	2203	2124
3.	The Behavior of the Glass Electrode in Non-Aqueous Media. V. Behavior of the Glass electrode in Glacial Acetic Acid. N. A. Izmailov and A.M. Aleksandrova	2207	2127
4.	The Problem of the Solubility of Complex Salts. K. B. Yatsimirsky	2213	2133
5.	The Thermochemistry of Ethylenediamine Complexes. K. B. Yatsimirsky and A.A. Astasheva	2219	2139
6.	Molar Structure and Boiling Points of Organic Compounds. VII. Boiling Points of Amines and Nitro Derivatives of the Methane Series. N. Kozlov	2225	2144
7.	The Condensation of Cycloolefins with Organic Acids. M. N. Tilichenko	2233	2152
8.	The Condensation of Benzyl Alcohol with Phenols. Yu. S. Zalkind and I.P. Kurlina	2239	2158
9.	Benzylation of Aromatic Hydrocarbons in Presence of Activated Clay. L. N. Petrova and O. V. Shvarts	2249	2168
10.	Acetylene Derivatives. 122. Mechanism of Hydration and Cyclization of Dieneynes. XXIX. Synthesis and Transformations of Vinylethynyl Borneol. I. N. Nazarov and M. S. Burmistrova	2255	2173
11.	Acetylene Derivatives. 123. Hydration of Isopropylvinylethynyl Carbinol to 2 methyl-5-isopropyltetrahydro-4-Furanone and 2-Isopropyl-Tetrahydro-4-Pyrone. I. N. Nazarov and S. S. Bakhmutskaya	2263	2179
12.	Acetylene Derivatives. 124. α-Ketoxides and their Transformations. I. The Oxidation of Mesityl Oxide and of 1-Methoxy 5 Methyl-4-Hexen-3-one to the Corresponding α-Ketoxides. I. N. Nazarov and A. A. Akhrem	2267	2183
13.	The Problem of the Estrogenic Activity of Anol and its Polymers. I. V. I. Maksimov, N. G. Yartseva, T. E. Zalesskaya and O. S. Madaeva	2279	2194
14.	The Condensation of py Indolealdehydes with Malonic Acid and Ethyl Cyanoacetate. V. M. Rodionov and T.K. Veselovskaya	2287.	2202
15.	The Relative Activity of Methyl Ketones. 1. Colorimetric Investigation of the Reactivity of Acetone and Acetophenone in Reactions with 2 Furaldehyde. V. I. Tikhonova	2299	2213
16.	Investigations in the Field of Polycyclic Compounds. XIII. The Absorption Spectra of Anthrapyridone-acridone, Anthraquinone acridone, Anthrapyridone and some of their Derivatives. A. M. Lukin, P. M. Aronovich and G. P. Brin	2305	2219
17.	The Transformation of Asymmetrical Dimethyldiphenylbutindiol in Acid Medium. I. The Isomerization of the Glycol under the Influence of an Alcoholic Solution of Sulfuric Acid. Yu. S. Zalkind E. D. Venus-Danilova and V. I. Ryabtseva	2309	2222
18.	The Transformation of Asymmetrical Dimethyldiphenylbutindiol in Acid Medium. II. The Condensation of the Glycol with Ethyl Alcohol in the Presence of Sulfuric Acid. E. D. Venus-Danilova and V. I. Ryabtseva	2317	2230
19.	The Reaction of the Esters of Cinnamic Acid with Isopropylmagnesium Bromide, Isobutylmagnesium Iodide and Bromide, n-Butylmagnesium Bromide and Phenyl Magnesium Bromide. A. D. Petrov and P. S. Bataev	2323	2236
20.	The Aromatization of 2 2 4-Trimethylpentane over Molybdenum Catalyst. A. F. Plate and O. A. Golovina	2329	2242
21.	The Preparation of Sulfamide. A. V. Kirsanov, Yu. M. Zolotov and N. L. Egorova	2339	2251
22.	The Thermal Condensation of Acetylene in the Presence of Porous Added Substances. A. F. Dobryansky and A. E. Drabkin	2345	2255
23.	The Polymerization of Vinyl Formate. A. A. Vansheydt and L. F. Chelpanova	2353	2261
24.	The Synthesis of N-(1-Naphthyl-4 Azobenzene)-Ethylenediamine, a Reagent for Penicillin. A. L. Yaroslavtsev	2367	2274
25.	A Colorimetric Method for the Quantitative Determination of Penicillin. A. L. Yaroslavtsev and A. N. Klimov	2373	2279
26.	The Dealkylation of β-(2-Alkoxynaphthoyl-1)-Propionic Acids and the Oxidation of β-(2 Ethoxynaphthoyl-1)-Propionic Acid. S. I. Sergievskaya and A. A. Chemerisskaya	2379	2284
27.	The Reactions of Aliphatic Diazo Compounds with Unsaturated Compounds. VI. The Ethyl Ester of 1-Acetoxycyclopropane-2 Carboxylic Acid. I. A. Dyakonov	2385	2289
28.	The Molecular Rearrangements of Organic Compounds in the Light of Butlerov's Theory of Structure. (To the Memory of A. E. Favorsky). S. N. Danilov	2397	2301
29.	The Synthesis, Structure and Transformations of β-2-Ethoxy-1(6)-Naphthoylpropionic Acids. S. I. Sergievskaya, A. V. Danilova and A. A. Chemerisskaya	2411	2314

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THE VISCOSITY OF BINARY MIXTURES CONTAINING NICOTINE. IV

S. F. Babak and V. V. Udovenko

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In preceding studies of this subject data were presented for the viscosity of binary systems of nicotine and aliphatic acids [1,2], and aromatic nitro derivatives [3]. Results are given in this paper of a study of the viscosity of binary systems containing nicotine and carbon tetrachloride, dichloroethane, chlorobenzene, and bromobenzene.

The compounds were first carefully purified and then had the following constants: b.p. of carbon tetrachloride 73.5° at 699 mm, of dichloroethane 80.5° at 704 mm, of chlorobenzene 127.5° at 701 mm, of bromobenzene 151.3° at 700 mm, and of nicotine 111-112° at 6 mm.

Results of the determination of the viscosity and density for the system nicotine – carbon tetrachloride are listed in Table 1, and the viscosity values are plotted in Fig. 1; the experimental data for the system nicotine – dichloroethane are given in Table 2 and the plot of the viscosity appears in Fig. 2; Table 3 relates to the system nicotine – chlorobenzene and Fig. 3 to its viscosity; Table 4 relates to the system nicotine – bromobenzene, and Fig. 4 to the corresponding viscosity plot.

TABLE 1

Nicotine – Carbon Tetrachloride

Mol % nicotine	Viscosity			Density		
	25°	35°	50°	25°	35°	50°
0.00	0.9240	0.7937	0.6607	1.5782	1.5578	1.5291
12.76	1.1979	1.0122	0.8402	1.4746	1.4606	1.4358
25.89	1.5456	1.2722	1.0011	1.3773	1.3607	1.3381
37.70	1.9146	1.5709	1.2156	1.3033	1.2898	1.2680
50.36	2.2747	1.8142	1.3693	1.2283	1.2179	1.1930
62.15	2.7032	2.1118	1.5023	1.1700	1.1559	1.1300
75.70	3.0763	2.3899	1.7311	1.1034	1.1096	1.0773
85.20	3.4054	2.6284	1.9065	1.0618	1.0518	1.0365
100.00	3.8942	3.1555	2.0376	1.0068	0.9986	0.9866

The viscosity diagrams of all the systems possess a similar form. At lower temperatures the viscosity isotherms are slightly convex to the composition axis, while at higher temperatures they are rectilinear. This shape of diagram points to the absence of interaction of the components, and it might be thought that dichloroethane, carbon tetrachloride, chlorobenzene and bromobenzene are indif-

TABLE 2

Nicotine - Dichloroethane (Ethylene Dichloride)

Mol. % nicotine	Viscosity			Density		
	25°	50°	75°	25°	50°	75°
0.00	0.7640	0.5549	0.4351	1.2486	1.2068	1.1676
12.12	0.9680	0.6903	0.5345	1.1917	1.1590	1.1227
25.33	1.2369	0.8640	0.6756	1.1495	1.1173	1.0879
37.80	1.5467	1.0393	0.7660	1.1107	1.0811	1.0572
50.60	1.8289	1.1703	0.8524	1.0835	1.0565	1.0295
64.74	2.4275	1.4864	1.0194	1.0555	1.0307	1.0050
77.10	2.8703	1.6918	1.1470	1.0328	1.0119	0.9895
89.36	3.4411	1.9268	1.2506	1.0193	0.9967	0.9745
100.00	3.8942	2.0376	1.2626	1.0068	0.9866	0.9670

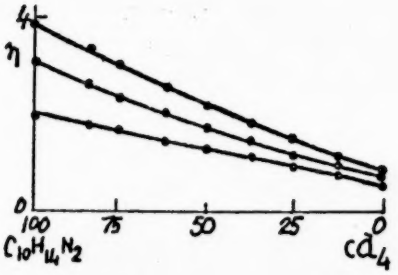

Fig. 1. Viscosity diagram of the system nicotine - carbon-tetrachloride.

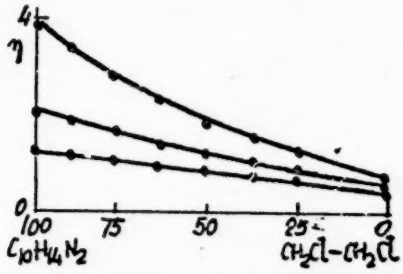

Fig. 2. Viscosity diagram of the system nicotine - dichloroethane.

TABLE 3

Nicotine - Chlorobenzene

Mol. % nicotine	Viscosity			Density		
	25°	50°	75°	25°	50°	75°
0.00	0.7424	0.5495	0.4342	1.0981	1.0709	1.0458
13.64	1.0044	0.7069	0.5339	1.0819	1.0571	1.0316
25.87	1.2057	0.8326	0.6090	1.0678	1.0440	1.0205
37.71	1.4951	1.0164	0.7309	1.0576	1.0326	1.0088
50.63	1.8380	1.1226	0.8140	1.0439	1.0196	0.9960
63.45	2.3135	1.4153	0.9806	1.0334	1.0107	0.9867
72.16	2.5972	1.5023	0.9950	1.0237	1.0023	0.9833
86.64	3.2115	1.8095	1.1272	1.0155	0.9939	0.9721
100.00	3.8942	2.0376	1.2626	1.0068	0.9866	0.9670

ferent toward nicotine. Such a conclusion, however, would only be correct in respect of chlorobenzene. Mixtures of nicotine and chlorobenzene do not change color on heating to 75°. Bromobenzene is next in reactivity: Its mixtures with nicotine acquire an orange color when heated to above 70°. Mixtures of nicotine with carbon tetrachloride begin to discolor even at 50°, while in the case of dichloroethane the color is intensified with rising temperature and becomes dark red at 75° after only a few minutes. Nicotine - dichloroethane mixtures

TABLE 4

Nicotine – Bromobenzene

Mol. % nicotine	Viscosity			Density		
	25°	50°	75°	25°	50°	75°
0.00	1.0619	0.7683	0.5941	1.4936	1.4589	1.4312
12.33	1.2333	0.9080	0.6950	1.4084	1.3793	1.3431
25.14	1.5435	1.0585	0.7871	1.3300	1.2986	1.2675
37.25	1.8303	1.1912	0.8500	1.2625	1.2338	1.2134
48.72	2.1909	1.3564	0.9562	1.2074	1.1800	1.1548
63.30	2.6039	1.5590	1.0391	1.1321	1.1101	1.0898
74.67	2.9670	1.6909	1.1034	1.0915	1.0703	1.0501
88.85	3.5249	1.9700	1.2596	1.0441	1.0190	0.9976
100.00	3.8942	2.0376	1.2626	1.0068	0.9866	0.9670

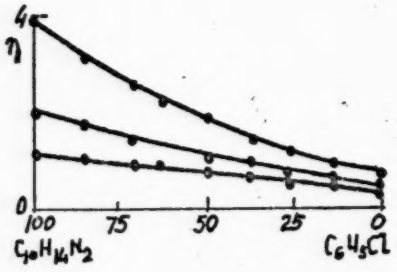

Fig. 3. Viscosity diagram of the system nicotine – chlorobenzene.

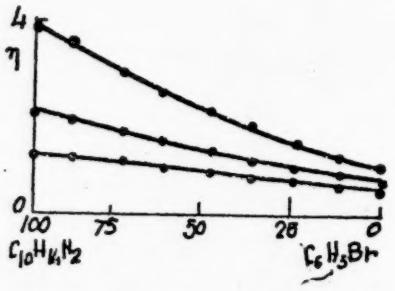

Fig. 4. Viscosity diagram of the the system nicotine – bromobenzene.

resinify after storage for a short period. This behavior indicates that dichloroethane cannot be considered completely inert toward nicotine.

SUMMARY

A study was made of the viscosity and density of the systems nicotine – dichloroethane, nicotine – chlorobenzene, nicotine – bromobenzene at temperatures of 25, 50, and 75°, and of the system nicotine – carbon tetrachloride at 25, 35, and 50°. In all of the systems the viscosity diagrams point to the absence of interaction of the components.

LITERATURE CITED

[1] S.F.Babak, J.Gen.Chem. 19, 1610 (1949).*

[2] S.F.Babak, J.Gen.Chem. 19, 1604 (1949). **

[3] S.F.Babak and V.V.Udovenko, J.Gen.Chem. 20, 1568 (1950). ***

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** CB translation p. a-23 ff.

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THE VISCOSITY OF SYSTEMS CONTAINING NICOTINE. V.

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In preceding papers in this field the results were presented of a study of the viscosity of binary systems of nicotine and aliphatic acids [1, 2], aromatic nitro derivatives [3], and some halo derivatives [4]. In the present paper re- results are reported of a study of the viscosity of binary systems of nicotine and acetone, methyl ethyl ketone and acetophenone.

TABLE 1

Nicotine – Acetone

Mol. % nicotine	Viscosity			Density		
	25°	35°	50°	25°	35°	50°
0.00	0.3332	0.3097	0.2725	0.7818	0.7706	0.7532
11.73	0.4615	0.4184	0.3526	0.8400	0.8289	0.8123
24.98	0.6975	0.6054	0.4988	0.8873	0.8722	0.8617
37.80	0.9326	0.7994	0.6476	0.9175	0.9057	0.8930
50.05	1.2797	1.0749	0.8411	0.9408	0.9295	0.9176
62.28	1.6955	1.3967	1.0648	0.9624	0.9517	0.9417
74.85	2.2737	1.8181	1.3637	0.9797	0.9725	0.9608
84.39	2.8560	2.2485	1.6[illegible]	0.9953	0.9834	0.9715
100.00	3.8942	3.1555	2.0376	1.0068	0.9986	0.9866

The substances used were first carefully purified and then had the following constants: acetone, b.p. 54.1° at 700 mm; methyl ethyl ketone, b.p. 77.3° at 705 mm; nicotine, b.p. 111-112° at 6 mm; and acetophenone, m.p. 20.5°

Results of measurement of the viscosity and density of the system nicotine – acetone are given in Table 1 and plotted in Fig. 1; those for nicotine – methyl ethyl ketone appear in Table 2 and Fig. 2; those for nicotine – acetophenone in Table 3 and Fig. 3.

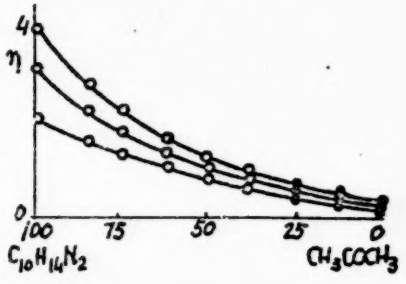

Fig. 1. Viscosity diagram of the system nicotine – acetone.

The viscosity isotherms of the system nicotine – acetone (Fig. 1) and the system nicotine – methyl ethyl ketone (Fig. 2) at all temperatures are convex to

TABLE 2

Nicotine – Methyl Ethyl Ketone

Mol. % nicotine	Viscosity			Density		
	25°	50°	75°	25°	50°	75°
0.00	0.4094	0.3203	0.2581	0.8004	0.7681	0.7438
12.53	0.5454	0.4075	0.3236	0.8467	0.8191	0.7937
24.63	0.7187	0.5104	0.3972	0.8822	0.8549	0.8324
36.42	0.9572	0.6647	0.4869	0.9104	0.8854	0.8634
48.78	1.2459	0.8283	0.5969	0.9395	0.9157	0.8934
61.33	1.6462	1.0414	0.7378	0.9602	0.9360	0.9144
73.74	2.2002	1.3158	0.8852	0.9801	0.9570	0.9361
88.30	3.0689	1.7675	1.1187	0.9969	0.9770	0.9552
100.00	3.8942	2.0376	1.2626	1.0068	0.9866	0.9670

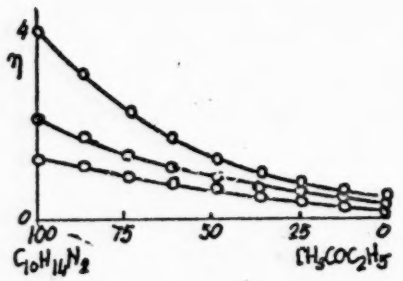

Fig. 2. Viscosity diagram of the system nicotine – methyl ethyl ketone.

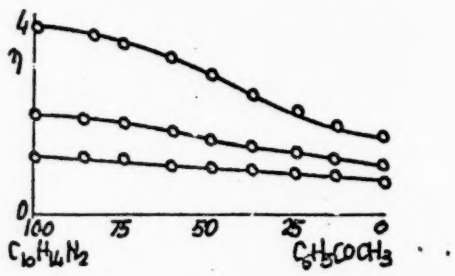

Fig. 3. Viscosity diagram of the system nicotine – acetophenone.

TABLE 3

Nicotine – Acetophenone

Mol. % nicotine	Viscosity			Density		
	25°	50°	75°	25°	50°	75°
0.00	1.6379	1.0507	0.7380	1.0242	1.0028	0.9814
13.32	1.8724	1.1618	0.7991	1.0225	1.0021	0.9781
24.26	2.1978	1.2880	0.8674	1.0222	1.0004	0.9780
37.82	2.5371	1.4526	0.9448	1.0197	0.9985	0.9767
49.34	2.9466	1.5514	1.0075	1.0162	0.9962	0.9748
61.30	3.2375	1.7426	1.0898	1.0140	0.9930	0.9722
74.31	3.6271	1.9115	1.1972	1.0118	0.9907	0.9710
84.02	3.7355	1.9624	1.2118	1.0100	0.9898	0.9697
100.00	3.8942	2.0376	1.2626	1.0068	0.9866	0.9670

the composition axis, suggesting the absence of interaction between the components. In the system nicotine – acetophenone (Fig. 3) the form of the isotherms is different; at a temperature of 75° the isotherm is rectilinear, while the isotherms at 50 and 25° are S-shaped. This form of isotherm points to interaction which is marked at 25°, becomes weaker with rising temperature and

substantially disappears at 75°. Examples are already known of reaction between ketones and organic compounds of a basic character. Thus, for example, acetone and aniline form an equimolecular compound existing in the liquid phase [5].

In a study of the viscosity of systems comprising ketones and organic acids, one of us [6] showed that reaction between ketones and organic acids is intensified on passage from acetone to methyl ethyl ketone. We see from the data of the present paper that nicotine reacts with acetophenone but not with acetone or methyl ethyl ketone. This is evidently bound up with the fact that the substitution of a CH_3 radical of acetone by C_6H_5 leads to weakening of the basic function of the ketone, with the result that interaction becomes possible.

SUMMARY

1. A study was made of the viscosity and density of the system nicotine – acetone at 25, 35, and 50°, and of the systems nicotine – methyl ethyl ketone and nicotine – acetophenone at 25, 50, and 75°.

2. Reaction between the components in the system nicotine – acetophenone was noted.

LITERATURE CITED

[1] S.F.Babak, J.Gen.Chem. 19, 1610 (1949).•

[2] S.F.Babak, J.Gen.Chem. 19, 1604 (1949).••

[3] S.F.Babak and V.V.Udovenko, J.Gen.Chem. 20, 1568 (1950).•••

[4] S.F.Babak and V.V.Udovenko, J.Gen.Chem. 20, 2121 (1950).••••

[5] G.Weibenberger, Fr. Schuster and J. Lielacher, Chem. Zentr., 1926, I, 2455.

[6] V.V.Udovenko and R.P.Airapetova, J.Gen.Chem. 9, 1162 (1939); 9, 1512 (1939); 9, 1564 (1939); V.V.Udovenko and R.P.Airapetova, J.Gen.Chem. 9, 1796 (1939); V.V.Udovenko and S.I.Batyaeva, J.Gen.Chem., 9, 1731 (1939).

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•See CB translationp. a-29 ff.

••See CB translation p. a-23 ff.

•••See CB translation p. 1629 ff.

••••See CB translation p. 2199.

THE BEHAVIOR OF THE GLASS ELECTRODE IN NON-AQUEOUS MEDIA

V. BEHAVIOR OF THE GLASS ELECTRODE IN GLACIAL ACETIC ACID

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This investigation is a continuation of a study of the properties of the glass electrode in non-aqueous media [1].

In the previous paper we reported a point of inflection in the calibration curve of a glass electrode of Hughes glass in the acid region. We suggested that this peculiarity in the behavior of the glass electrode would be more clearly manifested in acidic solvents. In the present investigation, therefore, we have examined the behavior of the glass electrode in acetic acid in the expectation that in this solvent deviations and inflection of the calibration curve at higher pH values would occur, coupled with the disappearance of the negative branch of the potential pH curve.

By virtue of its physical properties and its good solvent power, acetic acid is frequently used as a solvent. Hence the necessity for pH determination arises.

These pH measurements are generally carried out with the aid of the quinhydrone or chloranil electrode [2] (the chloranil electrode is an equivalent mixture of chloranil and hydrochloranil).

The chloranil electrode in acetic acid is less subject to oxidation than the quinhydrone electrode; however, its application, as well as that of the quinhydrone electrode, is attended by a number of difficulties.

The hydrogen electrode with platinum, both according to the literature [3] and our own observations, cannot be used in acetic acid. The best results are obtained by use of a gold electrode coated with palladium black [3].

Hence the use of the above-mentioned electrodes in acetic acid is limited. For this reason, as well as for the purpose of clarifying the character of the deviation of the glass electrode in acidic solvents, we have attempted to establish the practical possibility of utilization of the glass electrode in acetic acid for pH determinations.

EXPERIMENTAL

We used acetic acid from the Kharkov Reagent Factory in our investigation. Its purification by the usual method gave glacial acetic acid with $d_4^{17.5}$ 1.0533.

All of the measurements were performed on a potenticmetric apparatus with a radio tube (a detailed account of the apparatus appears in the paper by N.A. Izmailov and I.F.Zabara [4]). We used electrodes of the Haber type constructed of electrode glass prepared according to the recipes of Hughes and MacInnes and Dole, [5].

For the purpose of calibration of the glass electrodes, a series of solutions was prepared in glacial acetic acid solution with pH values of -1.4 to +8.3. The pH scale was calibrated against an infinitely dilute solution of ions of acid in acetic acid as the standard state.

Solutions with high pH values are solutions of dimethylaniline and sodium acetate in acetic acid; solutions with low pH values are solutions of chloric acid in glacial acetic acid. Still lower pH values were obtained by preparing strongly acid solutions by the method of Russel and Cameron [3] (solutions of sulfuric and chloric acids in glacial acetic acid with addition of acetic anhydride). We added 10% acetic anhydride and not 30% as recommended by the abovementioned authors.

The water added to the acetic acid together with the chloric acid combined with the acetic anhydride (due precautions being taken against explosion).

The compositions of the acetic acid solutions for calibration of the glass electrodes and their pH values are listed in the Table.

The pH values of the solutions in glacial acetic acid were determined with the quinhydrone electrode which was calibrated against 0.1437 molar H_2SO_4 in glacial acetic acid.

TABLE

No.	Composition of the solutions in glacial acetic acid	pH values
1	1-molar dimethylaniline	8.3
2	1.0 N CH_3COONa	8.1
3	0.25 N CH_3COONa	7.6
4	0.1 N CH_3COONa	7.25
5	0.01 N CH_3COONa	6.7
6	0.1 N CH_3COONa + ~ 0.1 N $HClO_4$ ..	6.3
7	0.05 N $HClO_4$	3.4
8	0.1 N $HClO_4$	2.1
9	0.2 N $HClO_4$	1.4
10	0.004 molar H_2SO_4 + 10% acetic anhydride	0.3
11	0.007 molar H_2SO_4 + 10% acetic anhydride	-0.2
12	0.02 N $HClO_4$ + 10% acetic anhydride	-1.4

Attempts to use HCl solution as a standard were unsuccessful because a solution of as little as 0.1 N HCl in acetic acid gives off fumes.

The pH of the standard was calculated from the formula

$$pH = - \log a = - \log m\gamma^*,$$

where a is the activity, m the concentration, and γ^* the activity coefficient related to an infinitely dilute solution in acetic acid as the standard.

The value of the activity coefficient of sulfuric acid in glacial acetic acid was taken from the paper of La Mer and Eichelberger [6].

Consequently the cell for determination of pH of acetic acid solutions contained no phase boundaries, and therefore no phase potentials. The magnitude of the pH was related to an infinitely dilute solution of the ions in the same solvent. Our scale is thus a specific scale: the scale zero was a solution of acid in acetic acid with an ionic activity of unity.

The range of such a scale for acetic acid is from a pH of 0 to 11.4 (the ionic product $k_i = 5.8 \cdot 10^{-11}$ [7]).

The glass electrodes prepared in the usual manner were first calibrated for aqueous solutions in the pH range of -0.4 to +13.85. For this purpose aqueous hydrochloric acid solutions, a series of buffer solutions according to MacIllvaine, Sörensen and Ringer, and sodium hydroxide solutions were prepared. The pH value

of the aqueous solutions was determined with the hydrogen electrode.

The calibration curves of the glass electrodes of Hughes and MacInnes glass against aqueous solutions are plotted in Figure 1.

Following this, the glass electrodes were calibrated against the acetic acid solutions. Measurements were made at 18-20° in the chain:

Hg	Hg_2Cl_2	Viebel's aqueous solution	Glass	Acetic acid solution under test	LiCl, 0.1 N in acetic acid	0.01 N HCl 0.09 N LiCl in acetic acid, quinhydrone	Pt

The siphon was filled with 0.1 N solution of lithium chloride in acetic acid. After each measurement the glass electrode was rinsed out with acetic acid. The potential of the glass electrode in acetic acid was rapidly steadied (in the course of 2-5 minutes) and subsequently remained constant. The potential only creeps in strongly acid solutions. Results of calibration of glass electrodes, constructed of two different glasses, against acetic acid solutions are plotted in Figures 2 and 3.

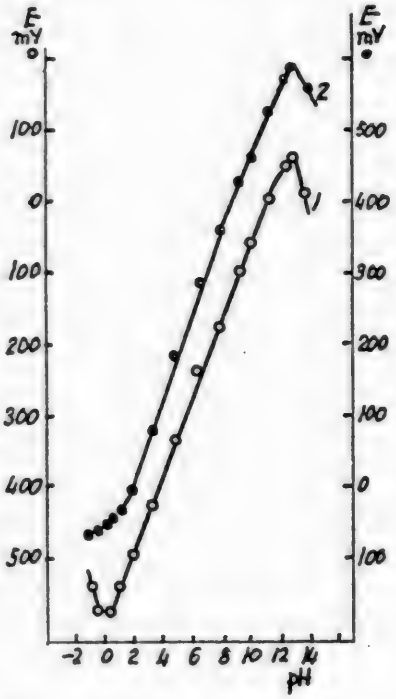

Fig. 1. Calibration curves of glass electrodes against aqueous solutions.

1-Hughes glass; 2-MacInnes and Dole Glass.

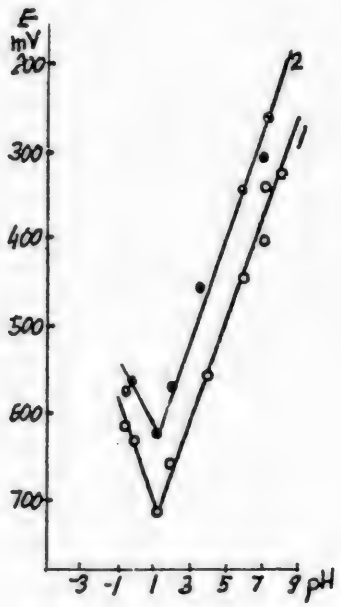

Fig. 2. Calibration curves of glass electrodes of Hughes glass against acetic acid solution.

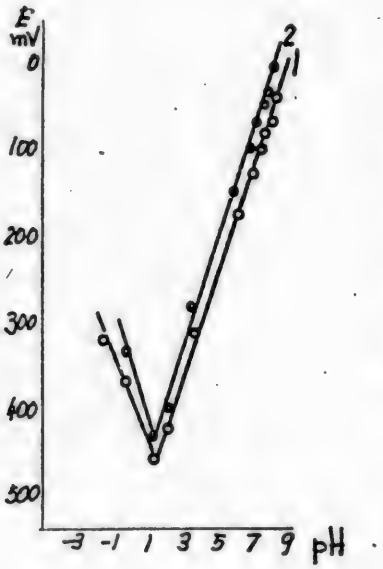

Fig. 3. Calibration curves of electrodes constructed of MacInnes and Dole glass against acetic acid solutions.

On comparing the calibration curves of glass electrodes in water and in acetic acid, we see that whereas an inflection point is observed at a pH of -0.2 for Hughes glass in acidic aqueous solutions, and merely a deviation from rectilinearity for Dole glass in the same pH region, in the acetic acid solutions

an inflection point is observed in the acidic region for both of the glasses at higher pH values of the order of +1.3. For Hughes glass the point of inflection is displaced by 1.5 pH units into the less acidic region, and the length of the negative portion of the calibration curve is increased in comparison with aqueous solutions.

As can be seen from the calibration curves for acetic acid solutions, between pH values of 1.5 and 8.5 (on the scale calibrated against the acetic acid standard) the potential of the glass electrode (constructed of both types of glass) changes rectilinearly with changing pH of solution.

We did not undertake studies in a more alkaline region since we could not attain higher pH values. Even a normal solution of sodium acetate in acetic acid has a pH of the order of 8, due to the low values of the activity coefficients of salts in acetic acid (dielectric constant of glacial acetic acid is 6.13 [8]).

The angular coefficient $\Sigma = \frac{\Delta E}{\Delta pH}$ in acetic acid solutions in the pH range of 1.5 to 8.5 has a mean value of 58.6 mV for Hughes glass and of 58.4 mV for MacInnes and Dole glass.

Consequently, for the acetic acid solutions which we examined in the pH range of 1.5 to 8.5 (on the scale related to the acetic acid standard) the glass electrodes may be used for measurements of acidity.

Reproducibility of Results During Measurements with the Glass Electrode in Acetic Acid

As is well-known, hysteresis is observed in the transition from alkaline to neutral solutions in aqueous and, particularly, in non-aqueous solutions. Hence, in order to assess the suitability of glass electrodes in acetic acid it was necessary to establish the degree of residual acidic hysteresis in the case of electrodes in acetic acid. With this objective in view, the electrodes were calibrated against acetic acid solutions starting from high pH values, and after the strongly acidic region they were at once again immersed in a solution with a pH of 8.3 and the series of measurements was repeated.

The experiment gave highly concordant results and pointed to the absence of residual acidic hysteresis in the alkaline region for glass electrodes in acetic acid.

The graphical representation of this double calibration in the case of Hughes glass electrodes is shown in Figure 4.

Immersion of the glass electrodes in water or measurement with the electrode of aqueous solutions immediately before measurements in acetic acid did not affect the electrode characteristics in acetic acid. This is clearly demonstrated in the following data for a Hughes glass electrode.

The values of E for a cell with a glass electrode in acetic acid solution with a pH of 6.05 are:

1. Immediately after keeping in water ..... 0.5980 V
2. After measurement in aqueous solution for a period of 20 min.. 0.5980 V
3. After measurement in aqueous solution for a period of 65 min.. 0.5985 V
4. After immersion in acidic acetate solution for 40 min..... 0.5980 V

It follows that the constants of the glass electrode in acetic acid do not depend on the duration of immersion of the electrodes in water or on the sequence in which measurements are made.

Titration in Acetic Acid with the Glass Electrode

It follows from the present investigation that the glass electrodes can be used for titration in acetic acid. As an example we describe the titration of a

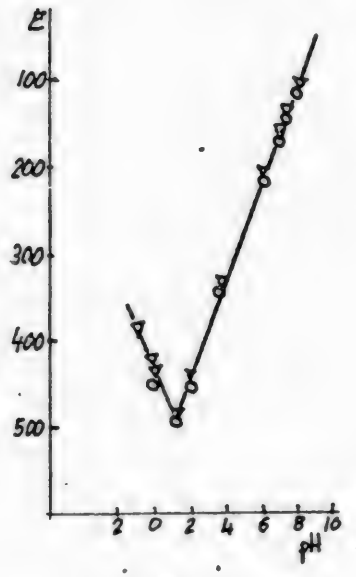

Fig. 4. Two repeated calibrations of a Hughes glass electrode.

On the graph the circles signify the first calibration and the triangles the second one.

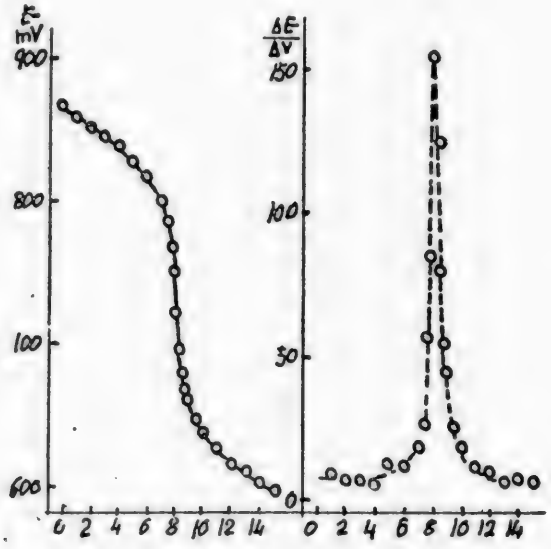

Fig. 5. Titration curves with a glass electrode in acetic acid.

solution of toluene sulfonic acid in acetic acid with an acetic acid solution of dimethylaniline, using a Hughes glass electrode.

Two calomel electrodes were included in the glass electrode cell:

Hg	Hg_2Cl_2	Veibel's aqueous solution	Glass	Acetic acid solution under test	Saturated aqueous solution of KCl	Hg_2Cl_2	Hg

As siphon we used an agar-water bridge.

Titration proceeded smoothly and rapidly. The potential was established in the course of two minutes. The titration curves are shown in Figure 5. The titration curve obtained by plotting EmV against the number of milliliters of added dimethylaniline solution is represented by the heavy graph.

The differential curve (plot of $\Delta E/\Delta pH$ against the number (V) of milliliters of added dimethylaniline solution) is represented by the broken line.

It can be seen that these curves are typical titration curves. We recommend the glass electrode for the titration of any desired compounds in glacial acetic acid.

SUMMARY

1. A study was made of the behavior of glass electrodes in glacial acetic acid.

2. The suitability of glass electrodes for pH measurements in acetic acid solutions was demonstrated.

3. It was found that the point of inflection in the acidic region in acetic acid is displaced in the direction of higher pH values in comparison with aqueous solutions, and the negative branch of the curve becomes longer.

4. Glass electrodes are shown to be suitable for potentiometric titration in acetic acid.

LITERATURE CITED

[1] N.A.Izmailov and M.A.Belgova, J.Gen.Chem. 8, 1873 (1938); N.A.Izmailov and T.F.Frantsevich-Zabludovskaya, J.Gen.Chem. 15, 283 (1945); 16, 301 (1946); N.A.Izmailov and A.M.Aleksandrova, J.Gen.Chem. 19, 1403 (1949).*

[2] A.M.Shkodin and N.A.Izmailov, J.Gen.Chem. 20, 39 (1950);** B.Heston and H.Hall, J. Am.Chem.Soc. 55, 4729 (1933); H. Hall and Werner, J.Am.Chem.Soc., 50, 2367 (1928).

[3] J.Russel and A.E.Cameron, J.Am. Chem.Soc., 60, 1346 (1938).

[4] N.A.Izmailov and I.F.Zabara, J.Phys.Chem.USSR, 20, 165 (1946).

[5] V.A.Pchelin, Measurements of the Activity of Hydrogen Ions with the Glass Electrode, Gizlegprom, Moscow (1941).

[6] V.K.La Mer and W.C.Eichelberger, J.Am.Chem.Soc., 54, 2763 (1932).

[7] S.Kilpi and W.M.Puranen, Z. Phys. Chem., Abt. A, 187, 276 (1940).

[8] B.Heston and H.Hall, J.Am.Chem.Soc., 54, 419 (1932).

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* See CB translation p. 1405 ff

** See CB translation p. 39 ff.

THE PROBLEM OF THE SOLUBILITY OF COMPLEX SALTS

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In collaboration with A.F.Kapustinsky [1] the fundamental relations governing the solubility of the simplest ionic compounds were previously discussed; at that time our considerations were based upon the correlations which we had established for the change of heat of solution of salts as a function of the ionic radii of their components [2] and of their entropies of solution. It was found that for salts of the type in question, the solubility is governed to a first approximation by the ratio of the ionic radii: minimum solubility is observed at a certain ratio of radius of cation to radius of anion (0.7 for the MX type and 1.1 for the MX_2 type).

Complex salts are composed largely of large ions which are weakly polarized with respect to each other; it can therefore be postulated that the laws derived for the simplest ionic compounds may be also in large measure applied to complex salts.

In fact, these conclusions are largely substantiated when we consider a series of complex salts with the simplest ions in the outer shell. In the case of salts of the KtX type (K^+ being a complex cation) the solubility invariably falls off in a series of salts with increasing radius of the anion (chloride – bromide – iodide; sulfate – chromate – bichromate; fluorosilicate – chloroplatinate, etc.). The radius of the complex ion is always somewhat large, and in the overwhelming majority of cases it exceeds 2 A; for this reason an increase in solubility in the series in question could only be anticipated when the ionic radius considerably exceeded 3 A.

On the other hand in the case of salts of the MX_2 type not only are series known in which the solubility decreases with increasing anionic radius, but also series with a solubility passing through a minimum. Since the minimum solubility is here reached at a ratio of atomic radii equal to 1.1, in the series chloride – bromide – iodide the least solubility will be manifested by the bromide when the radius of the cation is 2.2-2.3 A. Such a phenomenon is actually observed in the case of acidopentammine salts cobalt and iridium; the thermochemical radii of these salts is close to the stated value [3].

The radius of ions of the $[M(NH_3)_6]^{2+}$ type in the overwhelming majority of cases exceeds 2.6 A, and therefore the iodide should be the least soluble among the halide salts of this series. Our experiments have actually shown that in the case of hexammine nickel salts and triethylenediamine cadmium salts the solubility sharply decreases in passage from chloride to iodide.

Before passing to a consideration of some specific features of the solubility of complex salts, we propose to consider the influence of ionic charges on the solubity of the simplest salts.

With this objective we shall examine the equation

$$nRT \ln a = L + T\Delta S_p, \qquad (1)$$

in more detail. n is the number of ions forming a given salt; a is the activity of the salt in saturated solution; L is the heat of solution; ΔS_p is the entropy of solution of the salt.

We shall examine the change of solubility of salts in the KtX_n series (n = 1, 2, 3, etc.) with constant ionic radius.

The largest magnitude in Equation 1 is the heat of formation of the salt (L) which is related to the heats of hydration of the ions (L_k and L_A) and to the lattice energy of the salt (U) by the expression:

$$L = L_k + L_A - U. \qquad (2)$$

If we assume, in agreement with Mishchenko [4], that the heat of hydration of the potassium ion is 80 kcal, then the heat of hydration of the ions with identical radii will change in proportion to the square of the charge:

$$L_i = kz^2, \qquad (3)$$

where k is the proportionality coefficient and z is the ionic charge. The lattice energy of ionic compounds may be calculated with the help of Kapustinsky's equation [5]. On the basis of the foregoing considerations we obtain for salts of the KtX_n type:

$$L = A_1 z_k^2 + nA_2 z_A^2 - (n + 1)\, z_k z_A B. \qquad (4)$$

In this equation:

$$B = \frac{1}{r_k + r_A}\left(1 - \frac{0.345}{r_k + r_A}\right).$$

Taking into consideration the obvious relationship:

$$z_k = nz_A, \qquad (5)$$

we get:

$$L = A_1 z_k^2 + A_2 z_k z_A - Bz_k(z_k + z_A). \qquad (6)$$

For the purpose of investigating the dependence of L on the ionic charges, we differentiate Equation 6 with respect to z_k:

$$\frac{\partial L}{\partial z_k} = 2A_1 z_k + A_2 z_A - B(z_k + z_A) - Bz_k. \qquad (7)$$

Multiplying both sides of Equation 7 by z_k and taking Equation 6 into account, we get:

$$z_k \frac{\partial L}{\partial z_k} = L + L_k - \frac{Uz_k}{n + 1}. \qquad (8)$$

The various data at our disposal enable us to confirm that for small and medium-sized cations ($r_k < 1.6$ A) the term enclosed in brackets is positive, while for large cations it is negative to an extent increasing with decreasing size of anion. The heats of solution of complex salts constituted from large cations and anions are likewise negative.

The following conclusion may therefore be drawn: in the case of salts composed of large complex cations and large anions, the heats of solution decrease with increase of the charge on the complex ion when the dimensions of both of the ions remain constant.

Previously we had shown [1] that the entropy of solution decreases with increasing charge on the cation. Consequently, starting from Equation 1 we can also confirm that the solubility of complex salts of the KtX_n type decreases with increasing charge on Kt^{n+}.

The experimental data in the literature confirm the validity of this conclusion. Some examples in support are presented in Table 1.

TABLE 1

Solubility of Some Complex Salts in Water (in Moles per Liter) at 20°

Cations	Anions					
	Br^-	NO_3^-	I^-	Picrate	Naphthalene sulfonate	ClO_4^-
$1,2[Co(NH_3)_4(NO_2)_2]^+$	0.193	0.132	0.09	$15.8\cdot10^{-5}$	$89.5\cdot10^{-4}$	$5.86\cdot10^{-2}$
$[Co(NH_3)_5NO_2]^{2+}$	0.0436	0.0368	0.0945	$5.0\cdot10^{-5}$	$7.3\cdot10^{-4}$	$5.25\cdot10^{-2}$
$[Co(NH_3)_6]^{3+}$	0.04	0.033	0.015	$4.0\cdot10^{-5}$	$5.9\cdot10^{-4}$	$1.3\cdot10^{-2}$

It is clear from the equation given above that for the members of a given type of salts (KtX, KtX_2, etc.) the solubility of the salts decreases with increasing charge on both of the ions if they are sufficiently large. Thus, for example, the order of solubility of salts of the $Kt^{I}RO_n^{I}$ type is $10^{-2} - 10^{-1}$ moles per liter, that of salts of the $Kt^{II}RO_n^{II}$ type is $10^{-3} - 10^{-2}$ moles per liter, while that of $[Co(NH_3)_6]PO_4$ is $5.5\cdot10^{-4}$ moles/liter.

Up to now we have attempted to clarify the solubility relations of complex salts with the aid of equations strictly applicable only to specific monoatomic ions, and even this procedure yielded a series of rules which have proved useful in establishing, for instance, the least soluble combinations of ions.

Nevertheless, such a procedure does not take account of a whole series of complicating factors.

The shape of the ion exercises a marked influence upon the solubility of salts. A sharp deviation from a specific shape coupled with the absence of free rotation of the ion in a crystal leads, as we pointed out earlier [2], to a fall in the heat of hydration of the ion as compared with a specific ion characterized by the same thermochemical radius. The consequence of this, under otherwise identical conditions, is that salts containing ions deviating sharply from the specific form are less easily soluble than analogous salts composed only of spherical or, generally speaking, freely rotating ions.

Under the conditions favoring the occurrence of a chemical bond of the type of the hydrogen bond between a complex ion and molecules of water, the heat of hydration of the ion in question is greater than the heat of hydration of a simple ion with the same radius, since in this case a chemical effect is superposed on the electrostatic effect. In this connection the solubility of salts containing ions capable of forming a chemical bond with water molecules is higher than that of similar compounds incapable of chemical interaction with molecules of solvent.

From this standpoint, we obtain an explanation of the excellent solubility of hydrated salts, the majority of acid salts, salts of carboxylic acids, etc.

This also accounts for the well-known fact that the solubility increases in the series of salts:

$$[Co(NH_3)_6]X_3 < [Co(NH_3)_5H_2O]X_3 < [Co(NH_3)_4(H_2O)_2]X_3.$$

It can be confirmed that the presence in the complex ion of groups capable of forming a hydrogen bond (H_2O, OH^-, $RCOO^-$, etc.) leads to a sharp rise in solubility in comparison with compounds not containing such groups.

It follows that account should also be taken of the fact that the electric charges on a complex ion may be distributed unequally, resulting in a certain polarity inside the ions. The energy of interaction of such a complex ion with ions present in the outer shell increases even in the case of symmetrical distribution of the polar groups, as shown by calculations carried out by Khodakov [6].

The presence of polar groups in the complex ion leads to a higher lattice energy not only because of reaction of the polar ion with the outer shell, but also because of reaction between the multipoles of similarly charged ions. This effect possibly plays an even bigger part than the first one since in the overwhelming majority of cases the difference in solubility of salts containing ions approximately identical in size is much more strongly marked in the case of relatively small 'outer' ions. On the other hand, in the case of large ions present in the outer shell, the differences in solubility undergo variations (Table 2).

TABLE 2

Solubility of Acidopentammine Cobalt Salts (in Moles/Liter) at 20°

Anions	Cations			
	$[Co(NH_3)_5NO_2]^{2+}$	$[Co(NH_3)_5Cl]^{2+}$	$[Co(NH_3)_5Br]^{2+}$	$[Co(NH_3)_5I]^{2+}$
Cl^-	0.1078	0.0170	0.0106	0.0154
Br^-	0.0436	0.0178	0.00614	0.00076
NO_3^-	0.0368	0.0434	0.0107	0.00217
I^-	0.0945	0.0418	0.0101	0.0020
ClO_4^-	0.0525	0.0917	0.0837	–
SO_4^{2-}	0.0442	0.0344	0.0246	–
CrO_4^{2-}	0.0062	0.0074	0.0005	–

From the data of Table 2 we can conclude that, as a rule, with increasing thermochemical radius of the substituent X in the complex cation $[Co(NH_3)_5X]^{2+}$ the solubility of the corresponding salts decreases. All of the exceptions to this rule relate to salts with large anions in the outer shell where the differences in solubility of the salts are generally insignificant.

The solubility of complex ions is thus governed by the cumulative effect of a whole series of factors, and this fact makes it possible to utilize numerous complex ions of diverse types for the preparation of difficultly soluble combinations with most diverse ions bearing the opposite charge.

There are, however, types of complex ions differing from each other only in the nature of the central atom, for example:

$$[R(NH_3)_6]^{3+}, \quad [R(NH_3)_5Cl]^{2+}, \quad [R(NH_3)_5NO_2]^{2+}, \text{ etc.},$$

(R = Cr, Co, Rh, Ir, etc.). It may be thought that also in respect of the solubility of such salts a far-reaching analogy will also occur within numerous – groups. In the overwhelming majority of cases such an analogy actually occurs.

As an illustration we present in Table 3 the solubility data for various salts containing $[R(NH_3)_5Cl]^{2+}$ cations.

TABLE 3

Solubility of Complex Salts Containing Similar Ions (in Moles/Liter) at 20°

Cations	Anions		
	Cl^-	Br^-	NO_3^-
$[Co(NH_3)_5Cl]^{2+}$	$1.7 \cdot 10^{-2}$	$1.61 \cdot 10^{-2}$	$4.3 \cdot 10^{-2}$
$[Ir(NH_3)_5Cl]^{2+}$	$1.73 \cdot 10^{-2}$	$0.99 \cdot 10^{-2}$	$4.4 \cdot 10^{-2}$
$[Cr(NH_3)_5Cl]^{2+}$	$3 \cdot 10^{-2}$	-	$4.7 \cdot 10^{-2}$
$[Rh(NH_3)_5Cl]^{2+}$	$2.0 \cdot 10^{-2}$	-	-

On the basis of the foregoing considerations we may formulate in the following manner the conditions for preparation of difficultly soluble combinations with a given complex or, in general, large ion ($r > 2$ A): for the preparation of a difficultly soluble combination with a given large ion it is necessary to select a sufficiently large ion of opposite charge (maintenance of the optimum ratio of ionic radii) with the largest possible number of charges; furthermore, the composition of the given ion should not include hydrophilic groups (groups capable of forming a chemical bond with water molecules), and the presence of pronounced polarity within the ion is desirable.

The following anions, precipitants for complex cations, can be cited as examples: hexacyanoferrate, picrate, chloroplatinate, tetrathiocyanodiammine chromate, substituted sulfonates, etc.

Cations, precipitants for complex anions, can include cobaltiammine complex cations and large cations of organic bases.

The rules here formulated have been unwittingly applied in analytical practice. In a summary of microcrystalloscopic reactions I.M.Korenman [7] mentions about 180 reactions (out of a total of 680) based upon the unintentional application of the relationships here considered. However, their deliberate application may lead to the discovery of new analytical reactions.

SUMMARY

The fundamental factors governing the solubility of complex salts are considered: ionic dimensions and charges, the presence in them of polar and hydrophilic groups. Starting from the developed correlations, an explanation is put forward of the differing solubilities of some groups of complex salts, and the conditions for preparation of difficultly soluble complex salts are formulated.

LITERATURE CITED

[1] A.F.Kapustinsky and K.B.Yatsimirsky, J. Phys. Chem. USSR, 22, 1271 (1948).

[2] K.B.Yatsimirsky, Bull. Acad. Sci. USSR, Div. Chem. Sci., 398 (1948).

[3] K.B.Yatsimirsky and L.I.Pankova, J.Gen.Chem. 18, 2051 (1948).

[4] K.P.Mishchenko, Report to the Fourth Conference on the Chemistry of Complex Compounds, April, 1948.

[5] A.F.Kapustinsky, J.Gen.Chem. 13, 497 (1948).*

[6] Yu.Khodakov, Elements of Electrostatic Chemistry, G.T.I., Moscow-Leningrad, 1934.

[7] I.M.Korenman, Microcrystalloscopy, Moscow-Leningrad, 1947.

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* Evidently a typographical error, being either Vol. 13, 1943 or Vol. 18, 1948 (trans.).

THE THERMOCHEMISTRY OF ETHYENEDIAMINE COMPLEXES

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Ethylenediamine is an example of the extremely important and well-known addenda. Numerous complex compounds containing ethylenediamine are known and are characterized by varying degrees of stability. The thermochemistry of this important group of complexes has not been investigated at all thoroughly, and the results obtained by different authors have not been subjected to theoretical analysis.

The heats of formation of complex ethylenediamine salts of copper, zinc, cadmium, mercury, iron, and cobalt have been determined by Hieber and co-workers [1-5]. Some complex compounds of cobalt (III) with ethylenediamine have been studied from the thermochemical angle by one of us in collaboration with Pankova [6,7]; finally, two complex compounds of ethylenediamine with cobalt were studied by Ovenston and Terrey [8]. The heats of solution of ethylenediamine complexes have only been determined in isolated cases.

The investigation of the energy of addition* for some complex ethylenediamine ions and of the heats of addition of gaseous molecules of ethylenediamine to solid starting salts shows that the stability of ethylenediamine complex salts and that of the analogous ammoniates change in like measure. The stability of the complex ethylenediamine salts is always higher than that of the corresponding ammoniates.

Determinations have been made of the thermochemical constants of complex ethylenediamine salts of nickel and cadmium. The aims of this study were to check the above statement and to analyze theoretically the thermochemical data for the largest possible number of representatives of the group of compounds concerned. Another objective was the accumulation of additional thermochemical data for the ethylenediamine complex salts.

EXPERIMENTAL

The previously described [9] apparatus and methods were mainly used for the determination of the heats of solution and heats of reaction of the salts under investigation. A notable departure from the earlier procedure consisted in the use of a more sensitive thermometer and in a change in the method of introducing the weighed sample of salt into the calorimetric liquid. Temperatures were read with a Beckmann thermometer, the whole of the scale of which comprised one degree, and the accuracy of reading was $\pm$ 0.0002°. The test substance was introduced in a glass ampoule drawn out at the side into an extremely thin bulb. The bulb was crushed against the side wall of the calorimeter in the upper part of

*We denote by this term the heat of formation of a gaseous complex ion from a gaseous central ion and gaseous addenda.

the calorimetric liquid. By this procedure it was possible to shorten the principal period since a considerable proportion of the salt dissolved and did not fall to the base of the calorimeter. All of the measurements were performed at 25°.

The starting salts were prepared by the method described by Werner [10].

In all cases the determination of the thermochemical constants was preceded by a check of the purity of the prepared products by chemical analysis, when it was found that triethylenediamine-nickel iodide did not separate from aqueous solution as the monohydrate, as reported in the literature [10], but as the dihydrate. Dehydration of the ethylenediamine complexes of nickel was effected in a drying cabinet at about 100°.

The heat of formation of the enumerated salts was determined on the basis of measurement of the heat of reaction with 1 N HCl solution. A summary of the values obtained for the heats evolved during solution of the salts in hydrochloric acid appears in Table 1. The values obtained for the ethylenediamine complexes of $CdCl_2$ and $CdBr_2$ differ slightly from Hieber's values [5].

TABLE 1

Heats of Reaction of $[Nien_3]X_2$ and $[Cden_3]X_2$ with HCl

Compound	Weight, g	Change of temperature, in °, corrected for radiation	Correction	Heat capacity of the calorimeter	Heat of reaction	Mean value
$[Cden_3]Cl_2$ ...	0.4555	0.0899	0.0012	563.3	40.39	40.43
	0.7361	0.1457	0.0013	563.0	40.48	
$[Cden_3]Br_2$ ...	0.9740	0.1489	0.0004	563.7	38.97	39.02
	1.4371	0.2207	0.0010	563.8	39.03	
$[Nien_3]Cl_2 2H_2O$	0.3371	0.0583	0.0011	562.9	33.85	33.90
	0.4737	0.0772	0.0011	563.8	33.95	
$[Nien_3]Br_2$ ...	0.2900	0.0509	0.0001	538.4	37.64	37.64
$[Nien_3]I_2$	1.0167	0.1325	0.0016	539.1	35.40	35.41
	0.9782	0.1251	0.0012	563.3	35.47	
	1.0558	0.1345	0.0010	563.9	35.38	

The heats of solutions of all of the salts in water at high dilution were also measured, and the results are summarized in Table 2.

From our experimental data it appeared feasible to calculate the standard heats of formation of the investigated salts in the crystalline state and the heats of formation of the corresponding complex ions in aqueous solution.

The heats of formation of the crystalline salts were calculated from the equation:

$$[M(C_2H_8N_2)_3]X_{2(c)} + 6HCl_{aq} = M^{2+}_{aq} + 3C_2H_{10}N_2^{2+}aq + 6Cl^-aq + 2X^-aq + Q_1. \quad (1)$$

The heats of formation of all of the substances used and formed in accordance with Equation (1) are taken from Thermochemistry of Chemical Substances by Bichowsky and Rossini [11]. Moreover, all of the values given in that reference

TABLE 2

Heats of Solution in Water

Compound	Weight in g	Dilution	Change of temperature in °, corrected for radiation	Correction	Heat capacity of calorimeter	Heat of solution	Mean value
$[Nien_3]Br_2 \cdot 2H_2O$	0.7878	15300	-0.0484	0.0000	559.1	-14.83	-14.84
	0.6369	18900	-0.0390	0.0020	558.5	-14.85	
$[Nien_3]Cl_2 \cdot 2H_2O$	0.9070	10600	-0.0590	0.0000	559.2	-12.57	-12.59
	0.7041	13600	-0.0460	0.0000	558.8	-12.62	
$[Nien_3]I_2 \cdot 2H_2O$	0.9787	15000	-0.0500	0.0000	559.2	-15.07	-14.97
	0.8346	17600	-0.0420	0.0010	559.1	-14.88	
$[Nien_3]Br_2$	0.5422	20400	-0.0220	0.0000	558.8	-9.03	-8.91
	0.4110	26900	-0.0160	0.0000	558.7	-8.80	
$[Nien_3]Cl_2$	0.5642	15200	-0.0067	0.0000	558.8	-2.05	-2.26
	0.6397	13400	-0.0092	0.0000	558.9	-2.48	
$[Nien_3]I_2$	1.6934	8080	-0.0700	0.0000	560.0	-11.40	-11.39
	1.2805	10700	-0.0530	0.0000	559.6	-11.38	
$[Cden_3]Cl_2$	0.9212	10900	-0.0519	0.0005	564.2	-11.56	-11.56
$[Cden_3]Br_2$	0.9484	13500	-0.0481	-0.0008	564.2	-12.92	-12.92
	0.8258	15200	-0.0418	-0.0006	564.1	-12.92	

book were checked against the original sources. In the course of this check it was found that Bichowsky and Rossini cite an obviously erroneous value (-37.7 kcal) for $C_2H_{10}N_2^{2+}$; the heat of formation of the hydrated ethylenediaminium ion is actually 37.7 kcal. We eliminated this error from our calculations.

The heat of formation of the hydrated complex ion was determined from the magnitude of the heats of solution of the corresponding salts:

$$[M(C_2H_8N_2)_3]X_{2(c)} + aq = [M(C_2H_8N_2)_3]^{2+} aq + 2X^- aq + L. \qquad (2)$$

Incidentally this procedure provided a supplementary check on the values of the heats of reaction with HCl. The heat of formation of the complex ion in aqueous solution is bound to be constant, irrespective of the anion present in the outer shell.

In the case of $[Nien_3]Cl_2$, $[Nien_3]Br_2 \cdot 2H_2O$, and $[Nien_3]I_2 \cdot 2H_2O$, Equation (2) was used for calculation of the heats of formation of the crystalline salts under standard conditions.

Our values for the heats of formation of the investigated substances in the standard state are listed in Table 3.

TABLE 3

Heats of Formation of Complex Salts

Compound	Heat of formation (kcal)
$[Cden_3]Cl_2$	168.8
$[Cden_3]Br_2$	149.0
$[Nien_3]Cl_2$	163.1*
$[Nien_3]Br_2$	148.0
$[Nien_3]I_2$	119.6
$[Nien_3]Cl_2 \cdot 2H_2O$ ...	309.7
$[Nien_3]Br_2 \cdot 2H_2O$ ...	290.4*
$[Nien_3]I_2 \cdot 2H_2O$	259.9*
$[Cden_3]^{2+}aq$	78.3
$[Nien_3]^{2+}aq$	81.5

*Computation of the heats of solution of the salts in water.

EVALUATION OF RESULTS

In order to evaluate the stability of complex ions of the type in question we shall consider them in the gaseous state, thereby eliminating the influence of the outer shell and of the solvating effects bound up with dissociation of the complex ion in solution. We can then evaluate the energy evolved on addition of gaseous addenda (in this instance gaseous molecules of ethylenediamine) to the gaseous central ion, i.e., the energy change during the reaction:

$$M^{2+}_{(g)} + 3en_{(g)} = [Men_3]^{2+}_{(g)} + W. \qquad (3)$$

We call the energy change (W) during this reaction and other similar reactions the energy of addition.

Calculation of the value of W necessitates a knowledge of the heat of formation of all of the three types of particles taking part in reaction (3). For $Cd^{2+}_{(g)}$, $Ni^{2+}_{(g)}$ and $en_{(g)}$ these values are known with sufficient accuracy. The heat of formation of the gaseous complex ion $[Men_3]^{2+}_{(g)}$ may be calculated starting from the value of the lattice energy of the complex salt, i.e., the energy of the reaction

$$[Men_3]X_{2(c)} = [Men_3]^{2+}_{(g)} + 2X^-_{(g)} - U.$$

The lattice energy of the complex salt (U) can be calculated, as we have previously shown [12], with the aid of Kapustinsky's equation [13], utilizing the thermochemical radii of the ions [14]. The thermochemical radii of the ions may be calculated from the difference in the heats of formation of two salts containing an identical complex ion [14]. Applying this method in the present instance, we established that the thermochemical radii of ions of the type of $[Men_3]^{2+}$ do not differ among themselves within the limits of possible errors of determination of the thermochemical constants and are equal to 2.7 A.*

TABLE 4

Energy of Addition of Gaseous Molecules of Ethylenediamine and Ammonia to Gaseous Ions (in kcal)

Gaseous ions	Energy of addition		Difference
	3en	$6NH_3$	
Ni^{2+}	383	370	13
Zn^{2+}	372	366	6
Co^{2+}	372	359	13
Fe^{2+}	342	337	5
Cd^{2+}	323	311	12

On the basis of these data the heats of formation of the respective gaseous ions were calculated, and from these were found the energies of addition of the ions concerned. The energies of addition of ethylenediamine complexes and similar hexamminic ions are given in Table 4.

We see from the values in Table 4 that the energy of addition of three molecules of ethylenediamine to a gaseous central ion alters in the same order as the energy of addition of six molecules of ammonia. In all cases, however, the energy of addition of ethylenediamine exceeds that of ammonia by 5-13 kcal. Allowing for the possible error in the calculations, it may be assumed that this difference is approximately constant for all of the ions of the type considered.

It may therefore be suggested that in respect of the formation of ethylenediamine complexes the same forces come into play as in the case of formation of ammonia complexes, although the latter prove to be rather less stable.

The availability of data for the heats of formation of anhydrous and aqueous ethylenediamine complexes of nickel enables calculations to be made of the heats of hydration of salts of the type of $[Nien_3]X_2$. Values for these compounds are

*We had previously [4] calculated the heats of formation of gaseous ions of the halides, while the heats of formation of the crystalline complex salts are listed in Table 3 and in the above-cited literature sources.

presented in Table 5.

TABLE 5

Heat of Hydration of Triethylenediamine-Nickel Halides

Compound	Heat of hydration (kcal)
$[Nien_3]Cl_2 \cdot 2H_2O$ ..	10.3
$[Nien_3]Br_2 \cdot 2H_2O$ ..	5.9
$[Nien_3]I_2 \cdot 2H_2O$ ...	3.6

The unusual course of the heats of hydration is noteworthy: the heat of hydration increases in the order of iodide – bromide – chloride. Such an anomaly could only be explained on the assumption that the water molecules were coordinated round the anions, since it is scarcely permissible in the present instance to assume the presence of polarized ions or the development of covalent bonds between the complex ion and the halogen ion, which would lead, as we know, to "reversal" of the series.

SUMMARY

1. Heats of reaction with HCl solution were determined for the following complex salts: $[Nien_3]Br_2$, $[Nien_3]I_2$, $[Nien_3]Cl_2 \cdot 2H_2O$, $[Cden_3]Cl_2$, and $[Cden_3]Br_2$.

2. Heats of solution in water were determined for the following complex salts: $[Nien_3]Cl_2$, $[Nien_3]Br_2$, $[Nien_3]I_2$, $[Cden_3]Cl_2$, $[Cden_3]Br_2$, $[Nien_3]Cl_2 \cdot 2H_2O$, $[Nien_3]Br_2 \cdot 2H_2O$, and $[Nien_3]I_2 \cdot 2H_2O$.

On the basis of the data obtained, calculations were made of the heats of formation of the above salts and complex ions in aqueous solution, and also of the heats of hydration of complex salts of the type of $[Nien_3]X_2$.

3. Estimations were made of the thermochemical radii of ions of the type of $[Men_3]^{2+}$ and of the energy of addition of gaseous molecules of ethylenediamine to gaseous central ions. The occurrence was demonstrated of a parallelism in the changes of these values in the case of ethylenediamine complexes and ammoniates, and a greater degree of stability was observed in respect of the ethylenediamine complexes in comparison with the corresponding ammoniates.

LITERATURE CITED

[1] W.Hieber, H.Appel, Z. anorg. algem. Chem. 196, 193 (1931).

[2] W.Hieber, A.Woerner, Z.Elektrochem., 40, 252, 256 (1936).

[3] W.Hieber, E.Feder, Z. Elektrochem., 44, 881 (1938).

[4] W.Hieber, H.Appel, Z. Elektrochem., 40, 262 (1934).

[5] W.Hieber, E.Reindl, Z. Elektrochem., 46, 556 (1940).

[6] K.B.Yatsimirsky and L.L.Pankova, J.Gen.Chem. 19, 617 (1949). *

[7] K.B.Yatsimirsky and L.L.Pankova, J.Gen.Chem. 19, 623 (1949). **

[8] T.Ovenston, H.Terrey, J.Chem.Soc., 1936, 1660.

[9] K.B.Yatsimirsky and L.L.Pankova, J.Gen.Chem. 18, 2051 (1948).

[10] A.Werner, Z. anorg. Chem., 21, 201 (1899).

[11] F.Bichowsky, F.Rossini, The Thermochemistry of Chemical Substances, N.Y, 1936.

[12] K.B.Yatsimirsky, J.Gen.Chem. 17, 2019 (1947).

[13] A.F.Kapustinsky, J.Gen.Chem. 13, 497 (1943).

[14] K.B.Yatsimirsky, Bull. Acad. Sci. USSR, Div. Chem. Sci., 453 (1947).

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* See CB translation p. 569 ff.

** See CB translation p. 577 ff.

MOLECULAR STRUCTURE AND BOILING POINTS OF ORGANIC COMPOUNDS

VII. BOILING POINTS OF AMINES AND NITRO DERIVATIVES OF THE METHANE SERIES

N. Kozlov

Boiling Points of Amines of the Methane Series

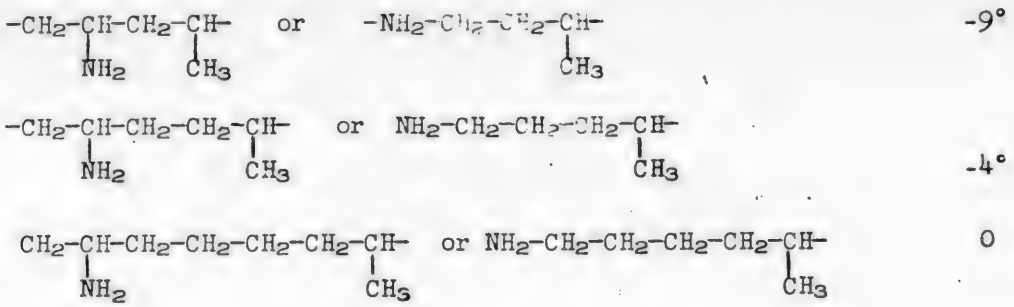
We are firmly convinced that the ideas developed by us in previous communications* on the basis of our procedure for studying the boiling points of various derivatives of the methane series made it possible to discover both the main laws governing their variations and the characteristic features typical of each specific class of compounds.

In the present paper we decided to apply our method to the study of the boiling points of nitrogenous derivatives of the methane series – the amines.

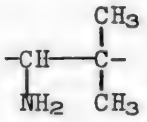
We first established the coefficients of the effects of structural factors on the boiling point. These have the following values.

Structural factor	Lowering of the b.p. compared to the b.p. of the compound with normal structure.
a) from the position of the NH_2 group in the chain:	
$CH_3-\underset{\displaystyle NH_2}{\underset{\vert}{CH}}-$	-12°
$CH_3-CH_2-\underset{\displaystyle NH_2}{\underset{\vert}{CH}}-$	-10°
and so on without change;	
b) from the position of the CH_3 group relative to the NH_2 group:	
$-CH_2-\underset{\displaystyle NH_2}{\underset{\vert}{\overset{\displaystyle CH_3}{\overset{\vert}{C}}}}-CH_2-$	-12°
$-CH_2-\underset{\displaystyle NH_2}{\underset{\vert}{CH}}-\underset{\displaystyle CH_3}{\underset{\vert}{CH}}-$ or $NH_2-CH_2-\underset{\displaystyle CH_3}{\underset{\vert}{CH}}-$	-9°

*N. Kozlov, Jour. Gen. Chem. USSR, 20, 1615, 1621, 1950. See CB translation p. 1675 and 1681 ff.



and correspondingly



-18°

etc.

The methyl groups present as substituents in the amine molecule exercise an influence on the boiling point when they are attached to carbon atoms; in that event their action causes a rise of 5° in boiling point.

Boiling points of amines of the aliphatic series were calculated with the aid of a formula previously proposed by us for the determination of the boiling points of various compounds of the aliphatic series and having the form:

$$T \text{ of iso structure} = T^1 \pm (a + b + c \ldots), \qquad (1)$$

where T^1 is the boiling point of a primary amine of normal structure, a, b, and c are the corresponding coefficients.

The calculations were based on the experimentally determined boiling points of amines of normal structure with the amino groups at the end of the chain, the data for which were taken from Beilstein and the values of which are listed in Table 1.

TABLE 1

Boiling Points of Primary Amines of the Methane Series with a Normal Structure

Name	Boiling point	Homologous difference
Methylamine	-6.7	-
Ethylamine	18.5	25.2
n-Propylamine	49.5	31.0
n-Butylamine	77.0	26.5
n-Amylamine	103.0	26
n-Hexylamine	129.0	26
n-Heptylamine	154.0	25
n-Octylamine	176.0	22
n-Nonylamine	196.0	20
n-Decylamine	216.0	20
n-Undecylamine	232.0	16

Applying formula (1) and the coefficients introduced in the present paper, we carried out calculations of the boiling points of amines of the paraffin series with an iso structure. Our results are listed in Table 2.

TABLE 2

Boiling Points of Primary Amines of the Aliphatic Series with an Iso Structure

Name	Boiling point		Name	Boiling point	
	Expt.	Calc.		Expt.	Calc.
Isopropylamine	31.5°	25.5°	3-Aminoheptane	–	144°
2-Aminobutane	66	65	4-Aminoheptane	141	144
1-Amino-2-methylbutane....	68	68	2-Amino-3-methylhexane..	–	133
2-Amino-2-methylpropane ..	45.2	53	4-Amino-2-methylhexane..	–	135
2-Aminopentane	90.2	91	3-Amino-2,2-dimethyl-pentane	–	126
3-Aminopentane	91	93	3-Amino-2,4-dimethyl-pentane	125	126
1-Amino-2-methylbutane....	95	94	2-Amino-2,4-dimethyl-pentane	121-122	121
2-Amino-2-methylbutane....	78	79	2-Aminooctane.....	164, 175	164
3-Amino-2-methylbutane....	84	82	3-Aminooctane	–	166
4-Amino-2-methylbutane ...	96	96	7-Amino-2-methylheptane.	168	168
1-Amino-2,2-dimethyl-propane	86	85	2-Amino-2-methylheptane.	–	152
2-Aminohexane	117	117	3-Amino-2-methylheptane.	158	157
3-Aminohexane	About 130	119	2-Amino-2,5-dimethyl-hexane.....	144	148
1-Amino-2-methylpentane...	–	120	2-Aminononane.....	69/11	184
2-Amino-2-methylpentane...	–	105	3-Aminononane	–	186
4-Amino-2-methylpentane...	103	108	4-Aminononane.....	–	186
5-Amino-2-methylpentane...	125	125	1-Amino-2-methyloctane..	185/186	187
1-Amino-2,2-dimethyl-butane 113-114		111	2-Amino-2,6-dimethyl-heptane	165-166	168
3-Amino-2,2-dimethyl-butane	101.5	99	2-Amino-2,7-dimethyl-octane	190	192
2-Amino-2,3-dimethyl-butane	104.5	101	3- or 4-amino-2,7-di-methyloctane	190-192	190
2-Aminoheptane	142	142	4-Amino-2,6-dimethyl-heptane	166-167	168
6-Amino-2-methylhexane	146	146	8-Amino-2,6-dimethyl-octane	202	199

The data of Table 1 form clear evidence of the fact that the influence of the homologous difference upon the boiling point likewise falls off smoothly in a homologous series of amines.

The data of Table 2, relating as they do to a considerable amount of factual material, confirm the suitability of our proposed formula (1) and of the coefficients for calculating the boiling point of amines with an iso structure.

The results of our calculations give an insight into the main systematic features of changes in boiling points in a series of amines which may be formulated as follows:

1) Transference of the amino group from the end or the start of the carbon chain to the interior of the chain brings about a regular depression of the boiling point of a perfectly specific magnitude equal to the values of our proposed coefficients.

2) In the interior of the molecule the amino group reacts with the methyl

groups which are present as substituents. The extent of this interaction is governed by their relative positions in the molecule; it is greater the closer these groups are to one another. Maximum interaction occurs when both of these groups are attached to the same carbon atom, while there is clearly no interaction when they are in the 1- and 5-positions in the molecule.

Interaction between amino group and methyl group affects the boiling point, causing a reduction by an extent equal to the above-enumerated coefficients, i.e., among the isomeric amines the amines in which the amino group is attached to a tertiary carbon atom will have the lowest boiling point. When interaction between the NH_2 and CH_3 groups ceases owing to increasing distance between them, interaction occurs between the terminal methyl group and the methyl groups which function as substituents in the case of compounds with a long chain.

The extent to which their interaction affects the boiling point will be subject to the same laws which were previously formulated by us for paraffinic hydrocarbons [1].

In the present paper we have introduced coefficients expressing the influence of reaction of the methyl groups which are substituents with terminal methyl groups with reference to compounds with a long distance between the methyl and amino group, as in 6-amino-2-methylhexane, 7-amino-2-methylheptane, and 8-amino-2,6-dimethyloctane.

On the basis of the laws so revealed, we are enabled to make some comments about the boiling points of amines of the paraffin series.

Firstly, the boiling point of 130° put forward for 3-aminohexane is wrong. The true boiling point of this compound is 119°.

Data in the literature about the boiling point of 2-aminooctane are extremely conflicting; according to the experimental data of one author its boiling point is 164°, while another author gives a value of 175°. Our calculations confirm that the true boiling point of 2-aminooctane is 164°.

Secondly, our proposed method makes it possible to carry out calculations of the boiling points of aliphatic amines which have not yet been synthesized, on the basis of their structural formulas.

The results of the calculations which have been made are presented in Table 2. We are of the opinion that our data will receive experimental confirmation in due course.

Boiling Points of Amines of the Olefinic Series

In contrast to the amines of the paraffinic series, the double bond enters as a structural factor in the amines of the olefinic series. In this case we make use of the concepts formulated under somewhat similar conditions for the course of the boiling points of olefinic alcohols, namely:

Firstly, the effects of the double bond and of the amino group separately upon the boiling point remain as previously enunciated in dependence on their position in the molecule and are governed by the coefficients which we previously derived for them.

Secondly, a methyl group (as substituent) attached to a carbon atom with a double bond does not react with the amino group no matter in which position the amino group occurs. This methyl group reacts only with a double bond, and the influence of this interaction on the boiling point is governed by the coefficients previously derived by us for these groups.

Thirdly, if the methyl group is attached to a carbon atom with a single bond, it reacts only with the amino group with an intensity depending upon their

relative positions in the molecule, and the influence of this reactivity on the boiling point is governed by the coefficients reported in this paper.

Fourthly, the amino group can react with a double bond only when it is attached to a carbon atom adjacent to a carbon atom with a double bond, i.e., in the position $-CH=CH-\underset{\underset{NH_2}{|}}{CH}-$, in these circumstances their interaction brings about a rise of 8° in the boiling point. This will also be the coefficient of their influence on the boiling point.

Fifth, an influence of methyl groups within the chain on the boiling point is observed when they are attached to adjacent carbon atoms.

The boiling points of amines of the olefinic series can be calculated with the help of our previous formula (1):

$$T \text{ of unsaturated amines} = T^1 \pm (a + b + c \ldots),$$

where T^1 is the boiling point of the saturated amine of normal structure with the same number of carbon atoms as in the unsaturated amine.

a, b, and c are the respective coefficients, the values of which were indicated above.

Applying the same procedure as with formula (1), we made calculations of the boiling points of amines of the olefinic series and present our results in Table 3.

TABLE 3

Boiling Points of Amines of the Olefinic Series

Name	Boiling point	
	Exper.	Calc.
Allylamine	53.6°	52.5°
4-Aminobutene-1	–	72
1-Aminobutene-2	85	85
3-Aminopentene-1	–	88
4-Aminopentene-1	85	86
5-Aminopentene-1	94	98
5-Aminohexene-1	117	115
5-Aminohexene-2	–	117
2-Amino-3-methylhexene-5	133	130
5-Amino-2-methylheptene-2	166	160
5-Amino-2-dimethylhexene-2	150	148
1-Amino-2-methylhexene-4	145	145
5-Amino-2-methylhexene-2	–	125
4-Amino-2-methylpentene-2	–	121
2-Amino-2-methylpentene-3	–	112

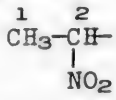
The data of Table 3 adequately confirm the accuracy of our calculations. They also enable us to state with confidence that the calculated boiling points of those unsaturated amines which have not yet been determined will receive experimental confirmation at a later date.

Boiling Points of Nitro Derivatives of the Paraffinic Series

In the first place we have established the effect of structural factors on the boiling point of nitro compounds of the paraffinic series. By the above-described method we obtained the following coefficients for various structural factors:

a) In dependence on the position of the nitro group in the carbon chain:

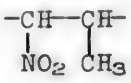
Depression of the boiling point



-12°

etc. without change.

b) In dependence on the position of the methyl group relative to the nitro group:



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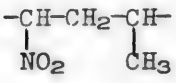

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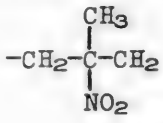
etc. without change;



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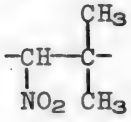

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The effect of interaction of methyl groups present as substituents remains as previously.

As in all of the previous cases the calculations were based on the boiling points of primary nitro compounds of normal structure. But the study of their experimentally determined boiling points convinces us that the boiling points of nitro compounds starting from nitroheptane have been quite inaccurately determined. This is evidently explained by their instability on distillation. Consequently, taking into account the regular manner in which the boiling point rises in passage from one homolog to another, we have calculated other values for a series of nitro compounds (Table 4).

TABLE 4

Boiling Points of Nitro Compounds With Normal Structure

Name	Experimentally determined boiling point	Homologous difference
Nitromethane ..	101	-
Nitroethane....	114	13
Nitropropane ..	130	16
Nitrobutane ...	151	21
Nitropentane ..	172	21
Nitrohexane ...	193	21
Nitroheptane...	193(213)*	20
Nitrooctane....	210-212(230)*	17
Nitrononane....	215-218(245)*	15
Nitrodecane	(260)*	15

*Our calculations

We subsequently applied formula (1) and our proposed coefficients to the calculation of the boiling points of compounds with a an iso structure. Results are presented in Table 5. The experimental values were taken from Beilstein.

The ample numerical material of Table 5 confirms the accuracy of our calculations. Therefore, in the series of nitro compounds of the paraffinic series

TABLE 5

Boiling Points of Nitro Compounds of the Paraffinic Series With Iso Structure

Name	Boiling point		Name	Boiling point	
	Expt.	Calc.		Expt.	Calc.
2-Nitropropane	117-120	118	2-Nitro-2,3-dimethyl-butane	170-174	169
2-Nitrobutane	139	139	3-Nitro-2,2-dimethyl-pentane	90/40	187
1-Nitro-2-methylpropane..	137-140, 158-159	144	2-Nitro-2,4-dimethyl-pentane	182	186
2-Nitro-2-methylpropane..	126	129	2-Nitro-2,5-dimethyl-hexane	201-202	203
2-Nitropentane.....	–	160	2-Nitroheptane	194-198	201
3-Nitropentane.....	155	160	2-Nitrooctane	210-212*	218
2-Nitro-2-methylbutane...	149-150	150	1-Nitro-2,7-dimethyl-octane	237**	248
3-Nitro-2-methylbutane...	–	153	2-Nitro-2,7-dimethyl-octane	235**	233
4-Nitro-2-methylbutane ..	150,164	167	1-Nitro-2-methylpentane..	–	186
2-Nitrohexane.....	176	181	1-Nitro-2-methylhexane...	–	206
2-Nitro-2-methylpentane..	172-176	171	2-Nitro-2-methylhexane ..	–	191
3-Nitro-3-methylpentane..	170-172	171			
3-Nitro-2,2-dimethyl-butane	167.5	167			

*Decomposes

**With decomposition.

we have likewise revealed the fundamental regularities of the change in their boiling points, i.e., among the isomers of nitro compounds the lowest boiling points will be possessed by those isomers in which the nitro group is attached to a tertiary carbon atom.

The laws which we have discovered enable us to confirm that of the conflicting experimental values for the boiling points of 1-nitro-2-methylpropane and 4-nitro-2-methylbutane reported by different authors, the most accurate will be those in agreement with our calculated values.

We also consider our formula and coefficients to be entirely suitable for calculation of the boiling points of those nitro compounds the boiling points of which have not been determined. And we are certain that the values obtained from our calculations will be confirmed experimentally.

Thus, our method has also proved suitable for the study of the boiling points of nitrogen-containing compounds of the aliphatic series and opens up the possibility of solution of a number of scientific and practical problems.

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THE CONDENSATION OF CYCLOOLEFINS WITH ORGANIC ACIDS

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The direct combination of organic carboxylic acids and olefins with formation of esters, discovered by D.I.Konovalov [1] as far back as the end of the last century, has received rather considerable attention in the patent literature during the past one-and-a-half decades, but the study of the fundamentals of the reaction has been neglected. Cycloolefinic hydrocarbons, for example, apart from cyclohexene, have been completely neglected in discussions on the problem.

We have found only four studies in the literature on the addition of cyclohexene to organic acids: Brunel [2] obtained the corresponding esters by heating cyclohexene with formic, acetic, and benzoic acids; Wunderly and Sowa [3] condensed cyclohexene with acetic acid in presence of various amounts of a molecular compound of boron fluoride and acetic acid and obtained cyclohexyl acetate; Zavgorodny [4,5] carried out this reaction in the presence of boron fluoride etherate.

In our investigation we have studied the influence in this reaction of chlorides of various metals, and also the action of phosphoric and sulfuric acids as catalysts. We have also studied the condensation of methyl-Δ^1-cyclohexene with trichloracetic acid.

No references were found in the literature to the condensation of this cycloolefin or of other homologs of cyclohexene with organic acids.

EXPERIMENTAL

1. Condensation of Cyclohexene with Acetic Acid

(with participation of L.V.Kachimova)

We prepared cyclohexene with b.p. 80-82° from cyclohexanone (b.p. 159-164°) by dehydration with sulfuric acid [6].

The following procedure was adopted: Into a series of test tubes, which were made ready for sealing, were introduced exactly weighed quantities of cyclohexene (0.200-0.2162 g), glacial acetic acid (0.1382-0.1437 g) and the substance destined for use as catalyst (10% of the weight of the first two components). The test tubes were sealed and heated at 97-100° in a drying cupboard fitted with a water jacket. After a definite interval of time the test tube and a blank were taken out, their contents quantitatively transferred to a measuring flask and diluted with water to the mark, and measured volumes of these solutions were titrated with 0.1 N baryta in presence of phenolphthalein. The per cent of combined acid was calculated from the difference in result obtained with the blank (this also

corresponded to the per cent yield of ester).

This method of calculation has been used by many workers (Konovalov [1], Timofeev [8], Zavgorodny [4,5,7], and others).

The metallic chlorides selected as catalysts were previously dehydrated by heating over a blowpipe. Those which were susceptible to hydrolysis were heated in admixture with ammonium chloride.

The results of the comparative experiments are shown in Table 1.

TABLE 1

Test No.	Catalyst	Duration (hours)	Ester formation
1	$ZnCl_2$.....	4	17.0
2	$AlCl_3$.....	4	14.0
3	$CdCl_2$.....	4	4.6
4	$CoCl_2$.....	4	5.6
5	$SrCl_2$.....	4	1.5
6	$NiCl_2$.....	4	0
7	LiCl.....	4	0
8	$FeCl_3$.....	4	0
9	$CeCl_3$.....	4	2
10	$SnCl_2$.....	4	0
11	50% H_2SO_4 ..	4	38.0
12	H_3PO_4 (1.83)	4	26.0

Table 1 shows that the most effective catalyst is 50% H_2SO_4, while the next best is H_3PO_4.

The following observations must be made concerning the metallic chlorides: in presence of $CdCl_2$, $CoCl_2$, $SrCl_2$, and $NiCl_2$, the reaction mixtures remained completely unchanged to the naked eye, and dilution with water was not followed by formation of precipitates; in presence of LiCl, $FeCl_3$ and $CeCl_3$ the reaction mixtures at the end of the experiment had acquired a light-brown color, and on dilution with water some gray (LiCl) or dark-colored flocs floated to the surface; in presence of $ZnCl_2$, $AlCl_3$, and $SnCl_2$, the reaction mixtures fairly quickly turned dark-brown and on dilution with water, in the last case, a relatively large amount of flocs rose to the surface, while in the other two cases an oily liquid with an ethereal odor appeared (the flocs might have dissolved in the oil).

Assuming the flocs to be polymers of cyclohexene, we can say that $SnCl_2$, while not manifesting any esterifying activity, is here a relatively powerful polymerizing agent.

$CoCl_2$ and $CdCl_2$ are noteworthy in that while exercising appreciable esterifying activity they are completely devoid of polymerizing and resinifying activity; under other conditions their esterifying activity might be enhanced.

Experiments with 50% H_2SO_4. It was noted above that 50% H_2SO_4 exhibited the most intense catalytic effect on the process of direct esterification of acetic acid by cyclohexene. In this connection experiments were undertaken with the aim of establishing the limiting value of this reaction. Results are listed in Table 2 and plotted in Figure 1.

It can be seen from Table 2 and Figure 1 that the reaction reaches a limit after approximately 8 hours, when the ester yield has risen to about 60%. Thereafter the ester yield falls, due presumably to increasing polymerization of the cyclohexene which is thereby irreversibly removed from the sphere of reaction, and the equilibrium of the process

$$C_6H_{10} + CH_3COOH \rightleftharpoons CH_3COOC_6H_{11}$$

is shifted to the left.

A fall in ester yields after attainment of a certain maximum was reported by Zavgorodny [7] for some aliphatic olefins on condensation with organic acids in presence of boron fluoride, and it was likewise explained by the intensification of polymerization of these olefins.

We may note further that in the condensation of cyclohexene with acetic acid in presence of boron fluoride, which latter is recognized as the most effective of all of the catalysts for this type of reaction described in the literature,

TABLE 2

Expt. No.	Temperature	Duration (hours)	Ester formation, %
1	97-100°	2	28.8
2	97-100	4	38.0
3	97-100	6	54.5
4	97-100	10	57.0
5	97-100	12	50.8
6	22-25	48	7.3

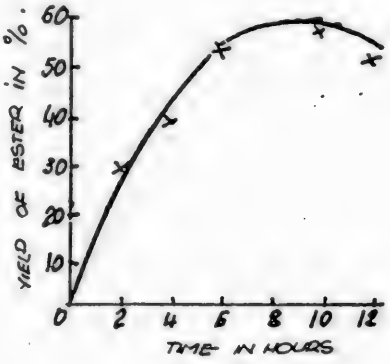

Fig. 1.

Zavgorodny [4] at 96-97° attained an ester yield of 60.5% after 73 hours and one of 61.5% after 118 hours from the start of the experiment; Wunderly and Sowa [3] at 80-82° obtained a 67% yield after 220 hours; in our experiments with 50% H_2SO_4 and at approximately the same temperature, a yield of the same order was attained after 8-10 hours.

In respect of ester yields during the condensation of cyclohexene with acetic acid, therefor, 50% H_2SO_4 is a no less effective catalyst than boron fluoride, and it is considerably superior to the latter in respect of reaction velocity.

The above-cited authors did not observe a fall in reaction limit in presence of boron fluoride [3,4]; but in presence of 50% H_2SO_4 the fall in ester yield becomes fairly conspicuous after only 12 hours from the start of the reaction.

Experiments with 98% H_2SO_4. The purpose of this series of experiments was to establish the direction of the effect of rise of concentration of sulfuric acid.

Experimental data for 98% H_2SO_4 are given in Table 3.

TABLE 3

Expt. No.	Temperature	Duration (hours)	Ester formation, %
1	22-25°	19	10.8
2	22-25	48	15.0
3	22-25	72	19.2
4	22-25	336	47.6
5	80-90	2	21.2
6	80-90	3	30.6
7	80-90	4	44.3

The data demonstrate that at room temperature the velocity of the reaction in presence of 98% H_2SO_4 is twice that in presence of 50% H_2SO_4:

50% H_2SO_4 after 48 hours yielded 7.3% ester (Table 2, Expt. 6);

98% H_2SO_4 after 48 hours yielded 15% ester.

This is likewise considerably higher than in presence of boron fluoride, as can be inferred from the condensation of cyclohexene with trichloracetic acid* in presence of boron fluoride etherate carried out at room temperature; the yield of ester here only attained 10.4% after 33 hours, and about 33.2% after 338 hours [4]. At a higher temperature there was a considerable difference between the reaction velocities in presence of 50 and 98% H_2SO_4.

*No experiments with acetic acid at room temperature have been reported in the literature. In the paper cited [4], however, it is shown that in the reaction with cyclohexene, trichloracetic acid surpasses acetic acid both in respect of velocity and reaction limit.

We were unable to establish the limiting values of the reaction in presence of 98% H_2SO_4 due to lack of cyclohexene.

2. Condensation of Methyl-Δ^1-cyclohexene with Trichloracetic Acid

(with participation of V.N.Sabinina)

Cyclohexene does not condense with trichloracetic acid in the absence of catalyst [4]. Methyl-Δ^1-cyclohexene differs conspicuously from cyclohexene in that a tertiary (non-hydrogenated) carbon atom is attached to the double bond. As exemplified by trimethylethylene, it has been established [1,8] that olefins of the aliphatic series containing a tertiary carbon atom at the double bond are capable of condensing at high velocity and with high yield with trichloracetic acid in the absence of catalyst.

It was undoubtedly of interest to compare cycloolefins in this respect with aliphatic olefins.

Methyl-Δ^1-cyclohexene was prepared by dehydration of o-methylcyclohexanone with sulfuric acid [6]; the ketone distilled almost completely at 166°, the temperature only rising to 168° at the end of the distillation.

The methyl-Δ^1-cyclohexene prepared for the experiments had the constants:

b.p, 106-108°; d_{20}^{20} 0.8026; n_D^{20} 1.4491.

These figures point to some contamination with methyl-Δ^2-cyclohexene.

Trichloracetic acid was first dried to constant weight in a vacuum desiccator over phosphorus pentoxide at 40-45°. Its degree of purity was determined by titration with 0.1 N baryta in presence of phenolphthalein.

Equivalent found 163.2 (for CCl_3COOH 163.5).

Experiments were performed by the previously described procedure. The only difference was that no catalyst was added to the reaction mixture, and at the end of the reaction the mixture was quantitatively transferred from the sealed test tube to a measuring flask by rinsing with benzene and the volume was also made up to the mark with benzene. The reaction components, as in the previous case, were used in equimolecular ratios. Experimental results are shown in Table 4 and Figure 2.

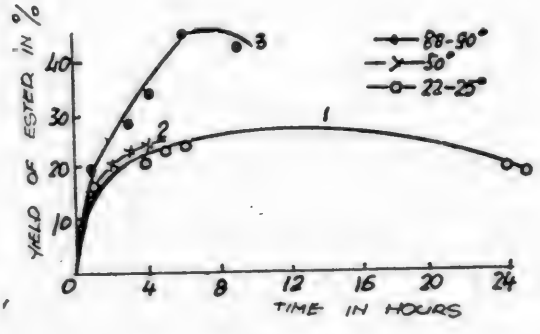

Fig. 2.

1 - 22-25°, 2 - 50°;
3 - 88-90°.

TABLE 4

Expt. No.	Temperature	Duration, hours	Ester formation, %
1	22-25°	1	16.9
2	22-25	2	17.9
3	22-25	4	21.1
4	22-25	5	23.1
5	22-25	6	24.4
6	22-25	24	20.3
7	22-25	25	19.1
8	50	2	20.4
9	50	3	22.8
10	50	4	24.1
11	88-90	1	20.1
12	88-90	3	28.3
13	88-90	4	34.3
14	88-90	6	45.5
15	88-90	9	43.4

We see from the data that cycloolefins with a tertiary carbon atom at the double bond, in contrast to cycloolefins with hydrogenated C-atoms at the double bond, are capable of combining with strong organic acids of the type of trichloracetic acid in the absence of catalysts.

The reaction as exemplified by methyl-Δ^1-cyclohexene proceeds fairly intensively even at room temperature, but by no means as energetically as in the case of hydrocarbons of the type of trimethylethylene.

According to the data of D.I.Konovalov [1] trimethylethylene and trichloracetic acid give the following yields of the corresponding ester:

at 18.5° after 0.5 hours, 75.5%; after 4 hours 85.3%; after 24 hours 89.9%; and at 99° after 0.5 hours 70.3%.

The reaction velocity increases slightly with rise of temperature. The limiting yield of ester at 88-90° is approximately twice as high as that at 22-25°, but is attained in about the same period of time as 22-25°.

Also noteworthy is the fact that with passage of fairly short intervals of time the limiting yields of ester begin to decrease significantly even at the ordinary temperature. We explain this phenomenon by the intensification of polymerization of the cycloolefin used, with consequent removal of the latter from the sphere of reaction. In this connection it is relevant to note that even at room temperature (22-25°) the reaction mixture turns light brown in the course of an hour. The color deepens nearly to black with prolongation of the reaction period; this process is markedly accelerated at high temperatures.

After removal of the aqueous portion from the benzene solutions of the experimental mixtures after titration, followed by drying of the solutions and removal of the benzene by distillation, there remained in the flask a soft vitreous mass with a light-brown color. When this was dissolved in 95% alcohol an abundant flocculent precipitate was formed. After the precipitate had been filtered off and washed with alcohol, it had a dirty-white color and did not react to the halogen test (Beilstein). It is presumably a polymer of our methylcyclohexene.

From the filtrate, on distillation of the alcohol, there remained 0.8 g of liquid which after distillation in vacuum, contained 1.5% less chlorine than is required by the methylcyclohexyl ester of trichloracetic acid. (The chlorine was determined by Stepanov's method.) For all of our 15 experiments (including blanks) we took about 4 g methyl-Δ^1-cyclohexene. Consequently, we were unable to isolate a large amount of ester, allowing for the yields which we obtained.

SUMMARY

1. Catalysts used in the condensation of cyclohexene with acetic acid were the chlorides: $ZnCl_2$, $AlCl_3$, $CdCl_2$, $CoCl_2$, $SrCl_2$, $NiCl_2$, LiCl, $FeCl_3$, $CeCl_3$, and $SnCl_2$; and also 50% and 98% H_2SO_4 and H_3PO_4 (sp. gr. 1.83).

2. Acids, especially sulfuric acid, were found to be more active catalysts for esterification than metallic chlorides.

The limiting yield of ester in presence of 50% H_2SO_4 at 97-100° was attained in 8-10 hours and was approximately 60%; longer heating periods reduced the yield.

According to the literature, in presence of boron fluoride, which is considered to be the best catalyst for condensation of olefins with organic acids, the yield of the same cyclohexyl acetate reaches 60-70%, but after a considerably longer period.

By using higher concentrations of H_2SO_4 the rate of esterification can be increased. The reaction limit under these conditions was not determined.

3. The most effective of the metallic chlorides proved to be $ZnCl_2$ and $AlCl_3$, the respective ester yields with which were 17 and 14% (after 4 hours at 97-100°).

$CoCl_2$ and $CdCl_2$ promote esterification but to an insignificant extent; they did not exhibit any polymerizing action upon cyclohexene.

In presence of $SnCl_2$, LiCl, $FeCl_3$, $CeCl_3$, $NiCl_2$, and $SrCl_2$ substantially no ester is formed. The last two exhibited no polymerizing action upon cyclohexene. Compared with the other salts, $SnCl_2$ has a stronger polymerizing action upon cyclohexene.

4. The reaction of methyl-Δ^1-cyclohexene with trichloracetic acid was studied without addition of catalysts at 22-25, 50, and 88-90°.

It was shown that trichloracetic acid begins to react with the hydrocarbon at the normal temperature. The reaction proceeds in two directions: Ester formation and hydrocarbon polymerization. The latter reaction is evidently responsible for the low limiting yield of ester (24.4% at 22-25° and 45.5% at 88-90°). The ester yield falls with prolongation of the reaction.

LITERATURE CITED

[1] D.I.Konovalov, J.Russ.Chem.Soc. 20, 594 (1888).

[2] L.Brunel, Ann. chim., (8) 6, 216 (1905); Chem. Zentr. 1905, II, 1938.

[3] H.L.Wunderly and F.J.Sowa, J.Am.Chem.Soc., 59, 1010 (1937).

[4] S.V.Zavgorodny, J.Gen.Chem. 14, 270 (1944).

[5] S.V.Zavgorodny, J.Gen.Chen. 14, 428 (1944).

[6] Adams and others. Organic Syntheses. T.Kh.TI, 1, 20 (1932).

[7] S.V.Zavgorodny, Trans. Voronezh State Univ., 10, 2, 41, 93 (1938).

[8] G.E.Timofeev and L.M.Andreasov, J.Russ.Chem.Soc. 47, 838 (1915).

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THE CONDENSATION OF BENZYL ALCOHOL WITH PHENOLS

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V.K.Teterin [1] has shown that when benzyl alcohol is heated in presence of catalysts - sulfanilic acid, activated clay or sulfuric acid - condensation products of two or more molecules of benzyl alcohol are obtained: benzyl ether, benzylbenzyl alcohol, and more complex products. The purpose of the present investigation is to study the action of the same catalysts on a mixture of benzyl alcohol and phenol and some of its derivatives.

Little work is recorded in the literature on the condensation of benzyl alcohol with phenol. It is known that the reaction yields p-benzylphenol in presence of zinc chloride, aluminum chloride or a mixture of glacial acetic acid and sulfuric acid. But we have been unable to find full details of the reaction products in these studies.

In our experiments we used a flask fitted with a thermometer and connected to a reflux condenser and a water trap, the volume of water serving as a measure of the reaction velocity. Benzyl alcohol and phenol were used in equimolecular quantities. Sulfanilic acid, activated clay (Chasov-Yar) and sulfuric acid served as catalysts. The solvent was benzene, by varying the amount of which we changed the boiling point of the mixture and consequently the reaction temperature.

Our experiments yielded a mixture of products. On the one hand, according to the observations of V. K.Teterin, the formation of dibenzyl ether, benzylbenzyl alcohol, and products of further condensation of these is possible. On the other hand, a primary product of condensation of benzyl alcohol and phenol should be phenylbenzyl ether, in addition to benzylphenol, since in the presence of sulfonic acids the alkylation of phenols may occur [2]:

$$C_6H_5CH_2OH + HOC_6H_5 \rightarrow C_6H_5CH_2-O-C_6H_5,$$

$$C_6H_5CH_2OH + C_6H_5OH \rightarrow C_6H_5CH_2C_6H_4OH.$$

Products of condensation of three molecules could also be formed - benzylphenyl benzyl ether or dibenzylphenol:

$$C_6H_5CH_2C_6H_4OH + HOCH_2C_6H_5 \rightarrow C_6H_5CH_2C_6H_4-O-CH_2C_6H_5,$$
$$C_6H_5CH_2C_6H_4OH + HOCH_2C_6H_5 \rightarrow (C_6H_5CH_2)_2C_6H_3OH.$$

The reaction products were separated and examined by the following procedure: The benzene and unreacted phenol and benzyl alcohol were distilled off with steam. Phenylbenzyl ether came over at the same time but to such a small extent as not to affect the calculation of reaction products. In a portion of the distillate the amount of phenol was determined in the form of tribromophenol. The total

distillate was then rendered alkaline to dissolve the phenol, and the amount of benzyl alcohol and phenylbenzyl ether was determined by extraction with ether and distillation in vacuum. The products which did not come over on distillation in steam were extracted with ether and distilled in vacuum for separation of the products of condensation of two and three molecules. A resin remained in the distillation flask – probably products of further condensation.

The phenols (o- and p-benzylphenols) were extracted from the products of condensation of two molecules by treatment with alkali, and were then fractionated, first by vacuum distillation, and then by boiling with a saturated solution of baryta water when the para isomer was precipitated and the ortho isomer remained in solution. By a special experiment it was established that under our conditions the phenylbenzyl ether did not isomerize to benzylphenol, so that the latter can be regarded as a primary product of our reaction.

The neutral products of condensation of two molecules were distilled in vacuum. Phenylbenzyl ether was determined as phenol after boiling with hydriodic acid, while the o- and p-isomers of benzylbenzyl alcohol were determined after conversion to o- and p-benzoylbenzoic acids by oxidation with nitric acid.

The products of condensation of three molecules were broken down by shaking with caustic alkali solution or by heating with 15% sulfuric acid, yielding phenol, benzylphenol, benzyl alcohol and benzylbenzyl alcohols. The quantitative composition of these products was accordingly determined from the decomposition products, although of course not altogether accurately.

The reaction in presence of sulfanilic acid was found to start at 130°, that using activated clay at 110°, and that with sulfuric acid at 83-85°. Judging by the separation of water, the reaction proceeds most rapidly of all with sulfuric acid and the most slowly with sulfanilic acid, although the latter gave the least resinification. The reaction velocity increases with rising temperature (being doubled after a 10° rise), but resinification is also intensified. Up to 80%, the amount of water separated is proportional to the time (the reaction is of zero order), but subsequently the reaction slows down.

In order to determine the yields of reaction products, experiments were performed with large amounts of initial products (150 g benzyl alcohol and 130.5 g phenol, i.e., 1.388 moles of each). Results are shown in Tables 1, 2, and 3.

TABLE 1

Catalyst	Amount reacted, %		Composition of reaction products, %		
	Phenol	Benzyl-alcohol	Formed by condensation of 2 molecules	Formed by condensation of 3 molecules	Resin
Sulfanilic acid	62.9	82.1	54.4	32.8	12.8
Activated clay	66.3	86.7	48.1	37.8	14.1
Concentrated sulfuric acid.....	72.7	94.7	45.6	32.1	22.3

It may be noted that with sulfanilic acid the p-isomers predominate. Thus, the benzylphenol contains 82.9% p- and 17% o-isomer. With sulfuric acid the o-derivatives predominate, while clay occupies an intermediate position with roughly equal quantities of o- and p- derivatives.

In all the cases the reaction proceeds to a greater extent at the expense of

TABLE 2

Products of Condensation of Two Molecules (in %)

Catalyst	Hydroxy derivatives			Ethers		
	Total	Benzyl-phenol	Benzylbenzyl alcohol	Total	Dibenzyl ether	Phenylbenzyl ether
Sulfanilic acid ...	53.0	44.6	8.4	47.0	28.8	18.2
Activated clay	85.1	78.1	7.0	14.9	14.9	Traces
Sulfuric acid	88.9	87.6	1.3	11.1	11.1	Traces

TABLE 3

Products of Condensation of Three Molecules (in %)

Catalyst	Dibenzyl phenol	o- and p- $C_6H_5 \cdot CH_2 \cdot C_6H_4OCH_2C_6H_5$	o- and p- $C_6H_5CH_2C_6H_4 \cdot CH_2OC_6H_5$	o- and p- $C_6H_5CH_2 \cdot C_6H_4CH_2 \cdot OCH_2C_6H_5$
Sulfanilic acid.....	–	35.0	25.65	39.35
Activated clay.....	4	54.3	27.5	14.2
Sulfuric acid	5	64.6	26.3	4.1

condensation of benzyl alcohol with phenol than in the direction of condensation of molecules of benzyl alcohol with each other.

Using sulfanilic acid, the total yield of ethers is 58.4% and that of hydroxy products is 28.8%; with sulfuric acid, on the other hand, hydroxy products are formed to a greater extent (42.1%) than ethers (35.56%); activated clay yields 42.4% hydroxy products and 43.5% ethers.

Experiments were also carried out with substituted phenols. It was found that under our conditions, tribromphenol and o-nitrophenol do not enter into reaction with benzyl alcohol. A little water is evolved when p-nitrophenol is heated with benzyl alcohol, but on working up the products about 90% of the nitrophenol is recovered unchanged, and the residue is a resin with the odor of benzaldehyde. Clearly condensation of the above-described type does not occur here, but some other reaction. p-Bromophenol and benzylalcohol reacted on heating in presence of sulfanilic acid, although with greater difficulty than in the case of phenol. The sole product of the reaction was p-bromophenylbenzyl ether.

These facts throw some light on the mechanism of the reaction under consideration. The formation of phenylbenzyl ether can proceed at the expense of the hydrogen of the phenolic hydroxyl group (scheme A) or as a result of fission of the phenolic hydroxyl group (scheme B):

(A) $C_6H_5-O-\boxed{H + OH}CH_2C_6H_5 \rightarrow C_6H_5OCH_2C_6H_5 + H_2O,$

(B) $C_6H_5-\boxed{OH + H}-OCH_2C_6H_5 \rightarrow C_6H_5OCH_2C_6H_5 + H_2O.$

In scheme A the introduction in the o- and p- position of substituents intensifying the acidic properties of phenol should facilitate the reaction, whereas in the case of scheme B such substituents should retard it.

The formation of benzylphenols proceeds at the expense of the hydroxyl group of benzyl alcohol and of the o- or p- hydrogen of the phenolic nucleus. The

hindering effect of the introduction of bromine may depend on the fact that the tautomeric effects of hydroxyl and bromine in the phenol molecule act in opposite directions.

The difficulty of benzylation of nitrophenols has also been noted by other authors: Baw [3] and A.E.Porai-Koshits [4].

EXPERIMENTAL

In order to study the possibility of condensation of two molecules of phenol, 20 g phenol, 15 ml benzene, and 0.1 g catalyst were heated to 140° with sulfanilic acid, to 120° with Chasov-Yar clay activated by the method of Tishchenko and Rudakov [5], and to 110° with sulfuric acid. In all of the experiments 19.7 g phenol was recovered unchanged, and no signs of reaction whatever were observed.

Condensation in Presence of Sulfanilic Acid

150 g benzyl alcohol, 130.5 g phenol (1.388 moles of each), 65 ml benzene, and 1.4 g sulfanilic acid were heated to 140° (thermometer in liquid), in a flask connected to a water trap and a reflux condenser. The rate of separation of water is shown in Table 4.

TABLE 4

Time from start of reaction (hours)	1	2	3	4	5	6	7	8	13
Water separated (in ml)	3.9	7.1	11	14.2	17.3	18.8	20	20.5	21.5

At the end of the reaction the benzene and phenol were distilled off with steam from the yellow liquid. 50 ml distillate (total 1675 ml) was taken for determination of the phenol. This sample yielded 5 g tribromophenol (m.p. 95°), from which it was concluded that the distillate contained 48.4 g phenol. Consequently 82.1 g phenol had entered into reaction.

The phenol in the distillate was brought into solution by addition of alkali. Extraction of the solution with ether gave 32.7 g substance which was also distilled in vacuum when 26.8 g was obtained with b.p. 92-96° (20 ml) and 3.6 g with b.p. 183-187°. The first fraction turned out to be benzyl alcohol (b.p. 204-206°; m.p. of the tetrachlorophthalate 134°), and the second phenylbenzyl ether (m.p. 38°, mixed melting test).

The products which did not distill in steam were extracted with ether, dried with potassium carbonate, and distilled in vacuum (20 mm) in quantity of 166.6 g.

First fraction: 173-210°, 91.9 g; second fraction: 220-269°, 54.2 g; residue (resin) 19.7 g.

The first fraction proved to be products of condensation of two molecules, and the second of three molecules.

0.3204 g fraction I. 24.39 g benzene: Δt 0.35°.
Found: M 191.
$C_{13}H_{12}O$. Computed: M 184; $C_{14}H_{14}O$ M 198.
0.2194 g fraction II. 26.50 g benzene: Δt 0.15°.
Found: M 281.
$C_{20}H_{18}O$. Computed: M 274; $C_{21}H_{20}O$. M 288.

Investigation of Products of Condensation of Two Molecules

The first fraction was worked up in the cold with 10% solution of potassium hydroxide. The undissolved products were extracted with ether. The alkali solution was acidified and the separated phenols were extracted with ether, dried with potassium carbonate and distilled at 3-4 mm, when 42.6 g phenols yielded 2 fractions: 156-158° (6.8 g) and 173-175° (30.4 g).

The first fraction was identified as o-hydroxydiphenylmethane from its boiling point and from the determination of the hydroxyl group by Tserevitinov's method. In order to remove the admixed p- derivative, we boiled it for 10 minutes with saturated barium hydroxide solution, filtered off the precipitate, acidified the filtrate, extracted the hydroxydiphenylmethane with ether and redistilled it. Crystals (5.7 g) were obtained with m.p. 21° which did not depress the m.p. of o-hydroxydiphenylmethane.

The second fraction was identified as p-hydroxydiphenylmethane (m.p. 83-84°, mixed melting test).

The alkali-insoluble products (42.3 g) were also separated into two fractions when distilled at 6-7 mm: 173-185° (19.9g) and 186-190° (14.8 g). The residue consisted of 6.9 g resin.

The first fraction did not contain hydroxyl; 2.5 g was boiled for 10 hours with hydriodic acid (b.p. 126°, 20 ml) and 2 ml glacial acetic acid. The mixture was diluted with water and distilled in steam. Treatment of the distillate with bromine water yielded 1.29 g tribromophenol, while oxidation of the filtrate with potassium permanganate give 1.3 g benzoic acid (m.p. 121°, mixed melting test). These data indicate that the first fraction contained 30% phenylbenzyl and 70% dibenzyl ether.

Analysis of the second fraction by the Tserevitinov method revealed the presence of 28-29.2% benzylbenzyl alcohol.

0.1218 g substance: 3.96 ml ethane (0°, 760 mm).
0.1126 g substance: 3.72 ml ethane (0°, 760 mm).
$C_{14}H_{13}(OH)$. Computed: 13.78 ml, 12.75 ml.

5 g of this fraction and 1 ml of water were heated on a water bath, and to the mixture was added dropwise, over a period of 2 hours, 15 ml nitric acid (sp. gr. 1.4).

At the conclusion of the reaction, the crystals were filtered off and washed with water; they were then repeatedly treated with boiling water, after which the residue was extracted with benzene. The still-warm aqueous solution deposited crystals of benzoic acid (m.p. 121°, mixed melting test). An amorphous precipitate came down when the solution was cooled. By repeated crystallization from water it yielded an insignificant amount of p-nitrophenol (m.p. 113°, mixed melting test). The residue after crystallization from xylene gave 0.02 g crystals with m.p. 125° (o-benzoylbenzoic acid melts at 127°).

The benzene solution yielded 0.32 g crystals which melted at 193° after several recrystallizations from benzene. On heating 0.17 g of this with 4 ml methyl alcohol and 0.1 ml sulfuric acid, a methyl ester with m.p. 107° was obtained. These data correspond to those of p-benzoylbenzoic acid. Consequently, this second fraction consists of o- and p-benzylbenzyl ether, dibenzyl ether, and a small quantity of phenylbenzyl ether.

Investigation of the Products of Condensation of Three Molecules

The product (b.p. 220-269° at 20 mm) was treated with a 10% solution of potassium hydroxide while stirring for a period of 6-8 hours. The phenols were

then separated from the neutral products in the usual manner. Distillation of the phenols (7.9 g) in vacuum (20 mm) yielded two fractions: 0.73 g, b.p. 80-85°, and 1.3 g with b.p. 180-200°. The first fraction was phenol (m.p. 41°, mixed melting test), and the second a mixture of p-hydroxydiphenylmethane (1.08 g) and hydroxydiphenylmethane which was purified in the manner described above. These products could have been formed only as the result of decomposition of the products of condensation of three molecules.

After two distillations at 6 mm the neutral products (44.3 g) gave the following fractions: 1) b.p. 81-83° (0.9 g), benzyl alcohol (tetrachlorophthalate, m.p. 134°); 2) b.p. 170-180° (4.6 g); 3) b.p. 210-220° (5.1 g); 4) b.p. 220-228° (8.2 g).

Investigation of the second fraction gave the following results:

0.1786 g substance: 0.5394 g CO_2, 0.1122 g H_2O.
0.2980 g substance: 23.20 g benzene: Δ t 0.33°.
Found %: C 84.74; H 7.33; M 198.4.
$C_{14}H_{14}O$. Computed %: C 84.78; H 7.12; M 198.1.

0.1142 g substance: 12.62 ml ethane (0°, 760 mm).
$C_{14}H_{13}(OH)$ Computed: 12.92 ml ethane.

This fraction is consequently a mixture of alcohols. For determination of their structure, 3 g was oxidized with nitric acid as previously described, and the products worked up as before to give benzoic acid. 0.3 g o-benzoylbenzoic acid (m.p. 125°, methyl ester, m.p. 51°) and 0.7 g p-benzoylbenzoic acid (m.p. 194°, methyl ester m.p. 107°). The first fraction is therefore a mixture of o- and p-benzylbenzyl alcohol.

The third fraction does not contain hydroxyl.

0.2406 g substance: 23.65 g benzene: Δ t 0.18°.
Found: M 288.
$C_{20}H_{18}O$. Computed: M 274.1.

This fraction is a mixture of ethers - products of condensation of three molecules. For determination of their structrue, 4 g of the fraction was heated for 2 hours with 100 ml of 15% sulfuric acid, and the phenols were then separated from the neutral products by the above method and identified. There was obtained 1.7 g phenols comprising 0.43 g phenol, 0.53 g p-hydroxydiphenylmethane, 0.14 g o-hydroxydiphenylmethane, and 0.5 g resinous substances. The neutral products, after distillation, yielded 0.54 g benzyl ether, 1.01 g of a mixture of o- and p-benzylbenzyl alcohols (judging by the products of oxidation) and 1.8 g resin.

Judging therefore by the products of decomposition, the ethers formed by condensation of three molecules have approximately the following composition:

o- and p-$C_6H_5CH_2C_6H_4CH_2$-O-C_6H_5 ..... 47.5%

o- and p-$C_6H_5CH_2C_6H_4CH_2$-O-$CH_2C_6H_5$ 11.3%

o- and p-$C_6H_5CH_2C_6H_4$-O-$CH_2C_6H_5$ 41.7%

The fourth fraction likewise did not contain a hydroxyl group.

0.6770 g substance: 20.69 g benzene: Δt 0.58°.
Found: M 288.
$C_{20}H_{18}O$. Computed: M 274; $C_{21}H_{20}O$, M 288.

The ethers were decomposed by heating on the water bath for 2 hours with a 10% alkali solution. Applying the above-described method, 5 g yielded 0.26 g p-hydroxydiphenylmethane, 0.02 g o-hydroxydiphenylmethane, 0.53 g benzyl alcohol, a trace of phenol, 2.7 g unchanged material, and 0.9 g resin. The fraction

accordingly has the approximate composition:

o- and p-$C_6H_5CH_2C_6H_4CH_2$-O-C_6H_5 ..... 3.8%,
o- and p-$C_6H_5CH_2C_6H_4CH_2$-O-$CH_2C_6H_5$ 67.5%,
o- and p-$C_6H_5CH_2C_6H_4$-O-$CH_2C_6H_5$ 28.8%

The total composition of the reaction products, calculated on the basis of the preceding data, is shown in Tables 1, 2, and 3. Since the structure of the products of condensation of three molecules obtained by us is based on the assumption that hydroxydiphenylmethane, like phenol, can only condense with benzyl alcohol and not with phenol, we tested this supposition by experiment. It was found that on heating a mixture of p-hydroxydiphenylmethane with phenol under our reaction conditions, the substances were recovered unchanged. On the other hand, on heating p-hydroxydiphenylmethane with benzyl alcohol, a mixture of ethers with a molecular weight of 262 was obtained, indicating that condensation had been effected.

Phenylbenzyl ether was recovered unchanged after heating with benzene and sulfanilic acid. The addition to the mixture of 5 g phenol, in order to simulate our reaction conditions more closely, did not result in any change. It follows, therefore, that hydroxydiphenylmethane was the primary product under our reaction conditions, and not the product of rearrangement of phenylbenzyl ether.

Condensation of Benzyl Alcohol with Phenol in Presence of Activated Clay

150 g benzyl alcohol, 130.5 g phenol, 75 ml benzene and 1.4 g activated clay (Chasnov-Yar) were heated in the usual apparatus at 120-121°.

TABLE 5

Time from start of experiment (hours)	1	2	3	4	5	6	7	7.5
Amount of separated water (ml)	6.6	13.2	18.8	22.1	23	23.6	23.8	23.85

The dark-red reaction products were investigated by the same method as for the reaction in presence of sulfanilic acid, and the isolated substances were identified by the same methods. There were obtained 44 g phenol and 19.8 g benzyl alcohol which had not reacted, 89.7 g of products of condensation of two molecules (b.p. 148-182° at 5 mm), 70.5 g of products of condensation of three molecules (b.p. 210-242° at 5 mm), and 22.8 g of resin.

The products of condensation of two molecules were found to consist of 70 g phenols and 18.8 g neutral compounds. The phenols were identified as a mixture of nearly equal amounts of o-hydroxydiphenylmethane (34.2 g) and p-hydroxydiphenylmethane (34 g). Distillation of the neutral portion at 10 mm yielded 2 fractions. The first (b.p. 148-149°, 5.3 g) mainly consisted of dibenzyl ether and a trace of phenylbenzyl ether. The second fraction (154-161°, 12 g) consisted, judging by the results of analysis by the Tserevitinov method and by the oxidation products, of a mixture of o- and p-benzylbenzyl alcohols (54% of this fraction) and dibenzyl ether.

The products of condensation of three molecules contained 4% in all of hydroxy compounds.

0.1048 g substance: 0.38 ml ethane (0°, 760 mm).
$C_{20}H_{17}OH$. Computed: 8.56 ml ethane.

The phenols were separated from the neutral compounds by treating the whole fraction with 10% sodium hydroxide solution while cooling and stirring. Even under these conditions a portion of the ethers was decomposed, as evident from the fact that fractionation of the phenols at 7 mm yielded 0.12 g phenol, 0.26 g p-hydroxydiphenylmethane, 0.12 g o-hydroxydiphenylmethane, and 0.9 g dibenzylphenol. The first three compounds are products of decomposition of ethers formed by condensation of three molecules. The dibenzylphenol was analyzed. It boiled at 231-233° (7 mm).

0.2168 g substance: 0.6934 g CO_2; 0.1260 g H_2O.
0.1640 g substance: 21.45 g benzene: Δt 0.14°.
Found %: C 87.22, H 6.50; M 279.
$C_{20}H_{18}O$. Computed %: C 87.54; H 6.62; M 274.
0.1752 g substance: 14.08 ml ethane (0°, 760 mm)
$C_{20}H_{17}OH$. Computed 14.32 ml ethane.

Distillation of the neutral compounds (63.2 g) at 10 mm gave 0.7 g benzyl alcohol, 1.1 g of a mixture of the o- and p-benzylbenzyl alcohols and 44.8 g (b.p. 210-246°) of a mixture of ethers containing 3 benzene rings.

0.3672 g substance: 20.84 g benzene: Δt 0.32°.
Found: M 281.
$C_{20}H_{18}O$. Computed: M 274; $C_{21}H_{20}O$. M 288.

Decomposition of the ethers by heating with sodium hydroxide and examination by the usual method gave (from 10 g of fraction): 0.36 g phenol, 1.2 g p-hydroxydiphenylmethane, 0.2 g o-hydroxydiphenylmethane, 1.01 g benzyl alcohol, 1.13 g of a mixture of o- and p-benzylbenzyl alcohols, 1.4 g of undecomposed product, and 2.9 g resins.

Calculation therefore gives the following approximate composition for the mixture of ethers:

o- and p-$C_6H_5CH_2C_6H_4$-O-$CH_2C_6H_5$ 56.6%

o- and p-$C_6H_5CH_2C_6H_4CH_2$-O-C_6H_5 ..... 28.6%

o- and p-$C_6H_5CH_2C_6H_4CH_2$-O-$CH_2C_6H_5$ 14.8%

The complete list of products appears in Tables 1, 2, and 3.

Condensation of Benzyl Alcohol with Phenol in Presence of Sulfuric Acid

150 g benzyl alcohol, 150.5 g phenol, 150 ml benzene, and 1.4 g sulfuric acid (sp. gr. 1.84) were heated to 95-96°.

TABLE 6

Duration of reaction (hours)	0.5	1	1.5	2	2.5	3	3.5
Amount of separated water, ml	5.6	11.1	16.5	21.9	23.1	23.6	23.9

The reaction mass turned brownish red. It was worked up by the previous method. 35.61 g phenol and 7.4 g benzyl alcohol did not react. Distillation at 6 mm yielded a first fraction of 94.8 g (158-181°), a second of 66.1 g (218-241°), and 45.7 g resins.

0.1538 g of first fraction: 17.63 g benzene: Δt 0.21°.
Found: M 187.
$C_{13}H_{12}O$. Computed: M 184; $C_{14}H_{14}O$. M 198.

0.2314 g second fraction: 19.42 g benzene: Δt 0.22°.
Found: M 276
$C_{20}H_{18}O$. Computed: M 274; $C_{21}H_{20}O$. M 283.

In the first fraction (products of condensation of two molecules) were detected phenols (61.4 g o-hydroxydiphenylmethane and 14.7 g p-hydroxydiphenylmethane) and alkali-insoluble compounds (10.4 g) comprising 11.3% o- and p-benzylbenzyl alcohols and 88.7% ethers. Decomposition of the latter with hydriodic acid did not give phenol, so that only dibenzyl ether had been formed.

The second fraction – products of condensation of three molecules – contained about 5% of hydroxy products. After treatment with caustic alkali and distillation of the alkali-insoluble products, there were obtained 0.14 g phenol, 0.3 g of a mixture of o- and p-hydroxydiphenylmethanes, 1.2 g compounds with b.p. 228-231° (at 5 mm) and 7.9 g resins.

0.1438 g substance: 0.4582 g CO_2; 0.0855 g H_2O.
0.2106 g substance: 18.43 g benzene: Δt 0.21°.
Found %: C 86.91; H 6.73; M 271.
$C_{20}H_{18}O$. Computed %: C 87.54; H 6.62; M 274.
0.2418 g substance: 18.9 ml ethane (0°, 760 mm) $C_{20}H_{17}OH$ computed 19.76 ml ethane.
This substance is therefore benzylphenol.

The alkali-insoluble components of the second fraction (52.4 g) gave on distillation (6 mm) 0.21 g benzyl alcohol, 0.36 g benzylbenzyl alcohol, and 37.2 g ethers (b.p. 207-243°) with a mol. weight of 284 and therefore containing 3 benzene rings. Distillation of 10 g of these ethers with sodium hydroxide yielded 0.46 g phenol, 0.5 g p-hydroxydiphenylmethane, 1.4 g o-hydroxydiphenylmethane, 1.37 g benzyl alcohol, 1.12 g of a mixture of o- and p-benzylbenzyl alcohols, 1.6 g undecomposed ethers and 3.1 g resins. These ethers therefore have the following approximate composition.

o- and p-$C_6H_5CH_2C_6H_4$–O–$CH_2C_6H_5$ 68%
o- and p-$C_6H_5CH_2C_6H_4$–O–C_6H_5 ..... 27.7%
o- and p-$C_6H_5CH_2C_6H_4CH_2$–O–$CH_2C_6H_5$ 4.3%

Experiments on the Condensation of Benzyl Alcohol with Substituted Phenols

Benzyl alcohol and nitrophenols. A mixture of 34.25 g p-nitrophenol, 27 g benzyl alcohol, and 40 ml benzene was heated for 7 hours at 145-150°. 2.8 ml water separated; dehydration of benzyl alcohol could yield 2.41 ml water. From the reaction mass were obtained 29.3 g p-nitrophenol and 13.7 g resins containing crystals of p-nitrophenol. Traces of benzaldehyde came over on distillation in steam.

Experiments with the same quantities and with addition of 0.4 g sulfanilic acid, 0.4 g of activated clay or 2 drops of strong sulfuric acid likewise resulted in up to 90% of the p-nitrophenol being recovered unchanged. A condensation reaction did not take place. Similar results were obtained with o-nitrophenol: less water separated than could result from the formation of dibenzyl ether, and nearly the whole of the o-nitrophenol was recovered.

Benzyl alcohol and bromo-substituted phenols. 16.5 g tribromophenol, 5.4 g benzyl alcohol, 15 ml benzene, and 0.1 g of catalyst were heated at 120-160°. With all of the three catalysts not more than 0.2 ml water separated, and 15.8-15.9 g tribromophenol could be recovered unchanged. A rather better reaction was obtained with p-bromophenol. 34.6 g bromophenol, 21.6 g benzyl alcohol, 20 ml benzene, and 0.28 g sulfanilic acid were heated for 1.5 hours to 140° when 2.7 ml water separated and the mass became dark-brown. The water had an acid reaction and gave a precipitate with silver nitrate. It was found to contain 0.039 g bromine. Benzene and benzyl alcohol were distilled off in steam, and the residue

distilled at 7 mm, yielding 20.1 g p-bromophenol, 16.3 g compound with b.p. 164-186°, 6.4 g with b.p. 190-240°, and 1.8 g resins.

The 164-186° fraction gave crystals which after crystallization from petroleum ether melted at 61° and were identified as p-bromophenylbenzyl ether. A mixture with p-bromophenol melted at 48°. The compound was odorless and insoluble in alkali.

0.2116 g substance: 0.4586 g CO_2; 0.0816 g H_2O.
0.1896 g substance: 0.1412 g AgBr.
0.2534 g substance: 17.65 g benzene: Δt 0.26°.
Found %: C 59.11; H 4.31; Br 30.25; M 262.
$C_{13}H_{11}OBr$. Computed %: C 59.31; H 4.21; Br 30.38; M 263.

The 190-240° fraction contained a total of 5% bromine and, judging by its molecular weight, was a product of condensation of 3 molecules of benzyl alcohol.

SUMMARY

Anhydrous sulfanilic acid, activated clay and strong sulfuric acid can serve as catalysts in the condensation of benzyl alcohol with phenols. Of the two possible reactions of condensation of molecules of benzyl alcohol with each other or with phenol, the second predominates in considerable measure. The resultant condensation products were investigated and illustrated the influence of the nature of the catalyst on the reaction course and on the composition of the products. The latter consist of a mixture of compounds containing 2 and 3 benzene rings. o- and p-Nitrophenols, likewise tribromophenol, did not condense with benzyl alcohol. A reaction takes place with p-bromophenol but with much greater difficulty than with phenol.

LITERATURE CITED

[1] J.Gen.Chem. 15, 109 (1945).

[2] H. Wuyts, Chem. Zentr. 1912, II, 1006.

[3] Baw, J. Indian Chem. Soc. 3, 101; Chem. Zentr. 1926, II, 1643.

[4] Trans. Leningrad Chem.-Tec. Inst. 1, 7 (1943); 3, 101; Chem. Zentr. 1926, II, 1643.

[5] J.Appl. Chem. 6, 691 (1933).

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BENZYLATION OF AROMATIC HYDROCARBONS IN PRESENCE OF ACTIVATED CLAY

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We have made a study of the dehydration of alcohols over various catalysts with the aim of using the reaction for quantitative determination. The amount of water evolved on dehydration served as a criterion of the alcohol content. Among the catalysts examined by us was an activated clay – askanite. In the case of benzyl alcohol the most rapid and most complete separation of water in presence of askanite was observed in a medium of aromatic solvents: benzene, toluene, xylene, cumene, and anisole. Alone or in solution in normal heptane, benzyl alcohol scarcely splits off water in presence of askanite, notwithstanding the similar temperature conditions. In this respect it resembles other primary alcohols. Dehydration of benzyl alcohol in the absence of solvents under the influence of acidic agents only yields solid resins. A detailed survey has been published [1] of work on the dehydration of benzyl alcohol alone.

V.K.Teterin [2] dehydrated benzyl alcohol in presence of activated clay in toluene solution and obtained liquid products, but explained their formation by polymerization of the benzyl alcohol alone. Yu.S.Zalkind and A.L.Kakhniashvili [3] were the first to recognize the possibility of combination of benzyl alcohol and aromatic compounds in presence of askanite. They reacted benzyl alcohol with resorcinol in benzene and isolated a solid product with m.p. 78° (benzylresorcinol).

They overlooked the possibility of reaction between benzyl alcohol and benzene although they also separated a fraction corresponding to diphenylmethane.

Our investigation of the products of the reaction has shown that benzylation according to the following general equation occurs when benzyl alcohol is heated with the above-mentioned aromatic compounds:

$$C_6H_5CH_2OH + C_6H_5R \longrightarrow C_6H_5CH_2C_6H_4R + H_2O.$$

The speed and completeness of the dehydration is accounted for by the benzylation reaction which depends not only on the mobility of the hydroxyl group of benzyl alcohol but also on the presence of a mobile hydrogen in the aromatic hydrocarbon resulting from the formation of a hydrocarbon-askanite complex. The more mobile the hydrogen atom in the para position to the substituent in the aromatic hydrocarbon, the greater the velocity of the reaction and the higher the yield. The importance of the mobility of the hydrogen atom is evidenced with special clarity when comparing the results of benzylation of cumene and anisole proceeding at one and the same temperature. The hydrogen in the para position of anisole is particularly mobile owing to the high degree of polarization of the molecule.

The following are the main products isolated after reaction of benzyl alcohol: In benzene – diphenylmethane; in toluene – 1-methyl-4-benzylbenzene; in m-xylene – 1,3-dimethyl-5-benzylbenzene; in cumene – 1-isopropyl-4-benzylbenzene; and in

anisole – 1-methoxy-4-benzylbenzene. Apart from these, dibenzyl derivatives were formed to a considerably smaller extent, for example dibenzyl in the case of benzene.

With the exception of the experiments with dimethylphenyl carbinol, solid resins are formed in all of the reactions. The quantity of these may be reduced with simultaneous increase in yield of the main product by using larger quantities of the hydrocarbon (see Table).

The loss of water in presence of askanite may be utilized for quantitative determination of benzyl and anisic alcohols and some tertiary alcohols in presence of primary saturated alcohols. Cyclohexyl carbinol, β-phenylethyl alcohol, and primary octyl alcohol do not give off water when heated in toluene in presence of askanite.

Allyl alcohol reacts only with anisole and is inert in benzene and toluene.

Influence of Amount of Hydrocarbon on Yield of 1-Methyl-4-benzylbenzene

Amount of toluene per 20 g benzyl alcohol	Yield of 1-methyl-4-benzyl-benzene	% yield on benzyl alcohol
20	6.5	20
50	9.2	28
100	13.5	41
200	16	50

We also examined the behavior of methylphenyl carbinol and dimethylphenyl carbinol, which can be regarded as benzyl alcohol in which one or two hydrogen atoms of the carbinol group are substituted by methyl groups, so that the alcohol function becomes secondary or tertiary. We wished to establish whether in these conditions water is simply split off with formation of unsaturated hydrocarbons or whether the alcohol residue combines with the aromatic hydrocarbon. Methylphenyl carbinol in both benzene and toluene yields products of substitution corresponding in physical properties to the respective unsymmetrical diphenylethanes.

The tertiary alcohol, dimethylphenyl carbinol, very quickly loses water (like linalool) when heated in presence of askanite, but forms products of condensation of two alcoholic residues, without substitution of the aromatic hydrocarbon used as solvent. Dimethylphenyl carbinol gives a hydrocarbon resembling that obtained by the action of phosphoric acid on this alcohol and to which the structure 2,5-diphenylhexene-2 has been ascribed [5]. Linalool gives, as the result of condensation of two alcohol residues, an aliphatic hydrocarbon, judging by the physical properties of the product formed. In contrast to the behavior of benzyl alcohol, the removal of water proceeds with the same velocity in solution in benzene and in petroleum ether.

Benzylation in presence of askanite may be recommended as a convenient method of synthesis of monosubstituted diphenylmethanes.

EXPERIMENTAL

1. Benzylation of benzene. Into a flask provided with a water trap and a reflux condenser were introduced: 200 g benzyl alcohol, 200 g benzene, and 20 g askanite. After boiling for an hour (temperature in the liquid 90°), 33 g of water was collected (1 mole). The catalyst was filtered at the pump and washed with benzene. Distillation of the benzene left 181 g of product which was distilled at 12 mm:

Fraction	B.p.	n_D^{20}	Wt. (g)
1	125-155°	1.537	50
2	155-200	1.567	8.7
3	200-217	1.5958	10
4	217-275		22
Residue			74

The first fraction solidified on cooling in ice and then melted at 16°. Diphenylmethane with m.p. 26° was isolated from it. From the fourth fraction, which solidified on standing, was separated 1,2-dibenzylbenzene (m.p. 78°) by recrystallization from alcohol.

2. Benzylation of toluene. Experimental conditions identical with those for benzene. The flask was charged with 200 g benzyl alcohol, 200 g toluene, and 20 g askanite. After driving off the toluene the product was distilled:

Fraction	B.p.	Weight, g	
1	121-122° (5 mm)	67.7	Intermediate fraction negligible
2	215-248° (20 mm)	54.7	
Residue		60.0	

After a second distillation two products were isolated:

a) 1-Methyl-4-benzylbenzene, $CH_3C_6H_4CH_2C_6H_5$:

b.p. 278-279°; n_D^{20} 1.5710; d_4^{20} 0.9958; M found 185, computed 182.

% C found 92.07, 92.38; computed 92.34.
% H found 7.45, 7.74; computed 7.66.
MR computed 59.65; found 60.13.

Oxidation with 1.5% permanganate solution gave p-benzoylbenzoic acid with m.p. 194-195° and an acid value of 231 (theoretical value is 248).

b) Dibenzyltoluene, $CH_3C_6H_3(CH_2C_6H_5)_2$:

b.p. 225-230° at 10 mm; n_D^{20} 1.6019; d_4^{20} 1.0482; MR found 88.38; computed 89.1.

% C found 92.64, 92.78; computed 92.60.
% H found 7.47, 7.48; computed 7.40.

3. Benzylation of m-xylene. Same reaction conditions. Charge: benzyl alcohol 30 g, m-xylene 130 g, and askanite 3 g. After driving off the xylene the product was distilled at 10 mm:

Fraction	B.p.	Weight, g
1	130-140°	6
2	140-150	23
3	150-250	4
Residue		3

The fraction boiling at 140-150° is identical with 1,3-dimethyl-5-benzylbenzene, $(CH_3)_2C_6H_3CH_2C_6H_5$, and after a second distillation it had the constants:

B.p. 130-132° at 6 mm; n_D^{20} 1.5700; d_4^{20} 0.9931; M found 194, computed 196.

Elementary analysis: % C found 92.29; computed 91.80.
% H found 8.27; computed 8.20.
MR computed 64.17, found 64.31.

4. Benzylation of cumene. Charge: benzyl alcohol 60 g, cumene 300 g, and askanite 6 g. Water was split off quantitatively in 75 minutes. The cumene was driven off and the product distilled at 10 mm:

Fraction	B.p.	Weight, g
1	up to 145°	6
2	145-151°	26
Residue		24

The second fraction, 1-isopropyl-4-benzylbenzene, $(CH_3)_2CHC_6H_4CH_2C_6H_5$, was distilled again:

b.p. 147-148° at 10 mm; n_D^{20} 1.5570; d_4^{20} 0.9697.

Oxidation with 1.5% permanganate solution gave p-benzoylbenzoic acid with m.p. 194° and acid value 250. According to the literature [4], 1-isopropyl-4-benzylbenzene has the constants:

B.p. 310° at normal pressure and 176° at 13 mm and d^{18} 1.007.

These data deviate from our own. Comparing our figures, however, with those reported for the closely related 1-propyl-4-benzylbenzene (b.p. 152-155° at 10 mm and d^{18} 0.9737), our data may be considered more accurate.

5. Benzylation of anisole. Same reaction conditions, using benzyl alcohol 30 g, anisole 150 g, and askanite 3 g. The product was distilled at 10 mm after the anisole had been driven off.

Fraction	B.p.	Weight, g
1	up to 153°	12.5
2	153-154°	25.2
3	154-156	3
Residue		7

The second fraction, 1-methoxy-4-benzylbenzene, $(CH_3O)C_6H_4CH_2C_6H_5$, had the constants:

B.p. 153-154° at 10 mm; n_D^{20} 1.5780; n_D^{20} 1.5780, d_4^{20} 1.0530. The content of methoxyl groups determined by the method of Viebock and Schwappach [5] was 14.5% (theoretical value 15.5%).

From the residue was isolated 2 g of substance boiling at 200-250° at 10 mm. Its methoxyl group content was 11.7% (dibenzylanisole requires 10.9%).

6. Experiments with phenylmethyl carbinol. These were performed under the conditions of analytical determination with 5 g alcohol and 50 g solvent in presence of 0.5 g askanite. The first experiment was carried out in toluene when 1 mole of water came off. The absence of unsaturateds in the reaction product (bromine number of 2) suggested that in this case again the alcohol residue had combined with the toluene. Distillation of the solvent was followed by isolation of 1.1 g of 1-phenyl-1-p-tolylethane, $CH_3C_6H_4-\underset{\displaystyle CH_3}{\underset{|}{CH}}-C_6H_5$

B.p. 151-156° at 10 mm, n_D^{20} 1.5680; d_4^{20} 0.9885.

A second experiment in xylene with the same proportions of reactants gave 1 g of 1-phenyl-1-m-xylylethane, $(CH_3)_2C_6H_3-\underset{\displaystyle CH_3}{\underset{|}{CH}}-C_6H_5$,

B.p. 150-160° at 10 mm; n_D^{20} 1.5590; d_4^{20} 0.9801.

7. Experiments with tertiary alcohols. a) Linalool. Reaction mixture: linalool 20 g, benzene 50 g, askanite 2 g. 1 mole water per mole alcohol was evolved in the course of 20 minutes. The benzene was distilled off and the product distilled at 9 mm:

Fraction	B.p.	Weight, g
1	up to 164°	4
2	164-169°	4
3	168-175	2
Residue		5

The second fraction had d_4^{18} 0.8442, n_D^{20} 1.5020; benzoic acid was not detected after oxidation with 1.5% permanganate.

b) Dimethylphenylcarbinol. The starting material contained about 20% acetophenone which under the reaction conditions did not enter into reaction and was recovered unchanged. 30 g of dimethylphenyl carbinol and 150 g of benzene were reacted in the presence of 2 g askanite. 1 mole of water was evolved per mole alcohol with exceptional rapidity. Removal of the benzene was followed by distillation at 10 mm:

Fraction	B.p.	Weight, g
1	82-85°	8
2	156-160	16
Residue		negligible

The second fraction was redistilled:

B.p. 164-166° at 13 mm; n_D^{20} 1.5675; d_4^{20} 0.9790.
Bromine number 66.55 (2,5-diphenylhexene-2 requires 67.5).
Period for complete bromination 36 hours.
% C calculated 91.46; found 91.90.
% H calculated 8.54; found 8.57.

The hydrocarbon obtained by the action of phosphoric acid on dimethylphenyl carbinol is reported in the literature to have b.p. 175° at 16 mm and d^{17} 0.9724.

The same hydrocarbon is obtained by dehydration of dimethyl carbinol in toluene.

SUMMARY

1. When benzyl alcohol and phenylmethyl carbinol are heated in presence of askanite in solution in benzene, toluene, xylene, cumene and anisole, the solvents are benzylated and one mole water is split off per mole alcohol.

2. When tertiary alcohols (linalool and phenyldimethyl carbinol) are heated with the above solvents in presence of askanite, water is split off only in the course of dehydration and no reaction with the aromatic compounds takes place.

3. Benzylation in presence of askanite can be used as a method of synthesis of monosubstituted diphenylmethanes and as a quantitative method for determination of benzyl alcohol, phenylmethyl carbinol and phenyldimethyl carbinol in presence of primary saturated alcohols.

LITERATURE CITED

[1] R.L.Shriner, A.Berger, J. Org. Chem. 6, 305 (1941).

[2] B.K.Teterin, J.Gen.Chem. 15, 109 (1945).

[3] Yu.S.Zalkind and A.L.Kakhniashvili, Trans. Tbilisk State Univ., XXXa, 1947.

[4] A.Klages, P.Alendorf, Ber., 31, 998 (1898).

[5] A.Klages, Ber., 35, 2633 (1902).

[6] F.Viebock, A. Schwappach, Ber., 63, 2818 (1930).

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ACETYLENE DERIVATIVES

122. MECHANISM OF HYDRATION AND CYCLIZATION OF DIENEYNES.

XXX. SYNTHESIS AND TRANSFORMATIONS OF VINYLETHYNYL BORNEOL

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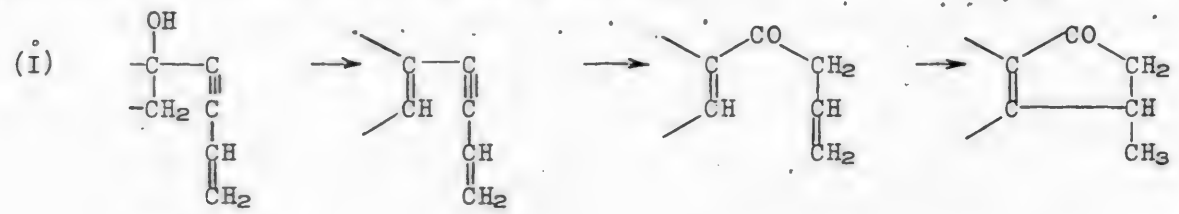
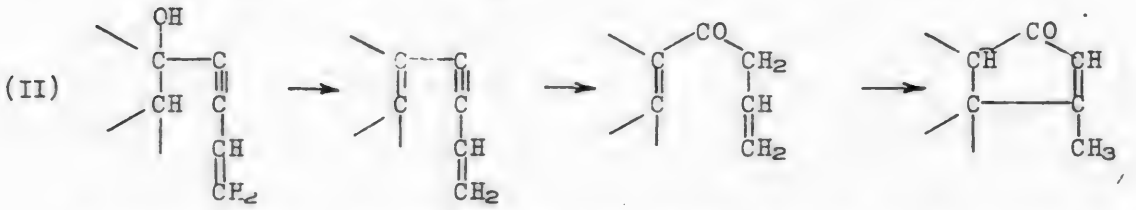
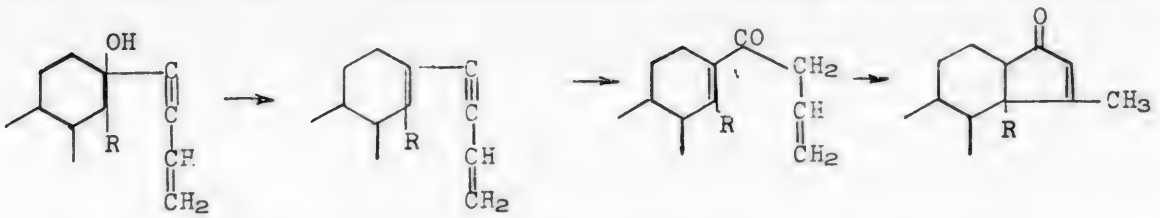
In preceding studies by our laboratory it was shown that the most diverse vinylethynyl carbinols can be readily transformed into the corresponding cyclopentenones by one of the following two schemes:



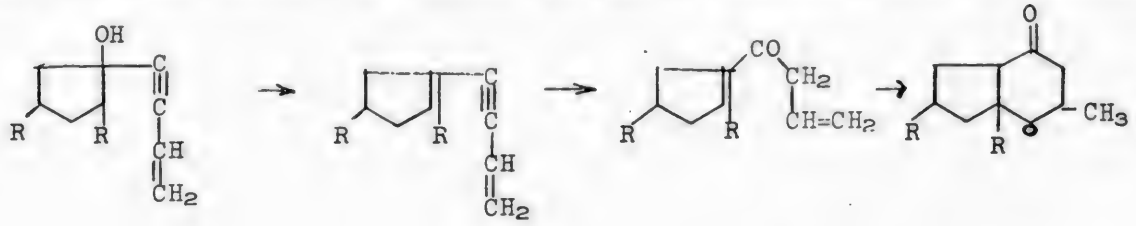


In transformations illustrative of the first scheme, the cyclization of vinylallyl ketones is effected at the expense of the free hydrogen of the vinyl group and leads to the formation of substituted $\Delta^{1,2}$-cyclopenten-5-ones [1]. The basis of the second scheme is the cyclization of vinylallyl ketones not possessing free hydrogen atoms in the vinyl radical; cyclization is then effected at the expense of the free hydrogen of the allyl group and leads to formation of substituted $\Delta^{3,4}$-cyclopenten-5-ones [2].

The application of these transformations to the cyclization of vinylethynyl carbinols makes possible the preparation with extraordinary ease of polycyclic ketones containing the cyclopentenone nucleus as well as angular substituents [3].



An interesting exception to these transformations is represented by the behavior of allyl-Δ^1-cyclopentenyl ketones which have proved to be completely resistant to cyclization by the usual reaction to the corresponding cyclopentenones (bicyclooctenones), but instead are readily hydrated to bycyclic pyrones [4]:

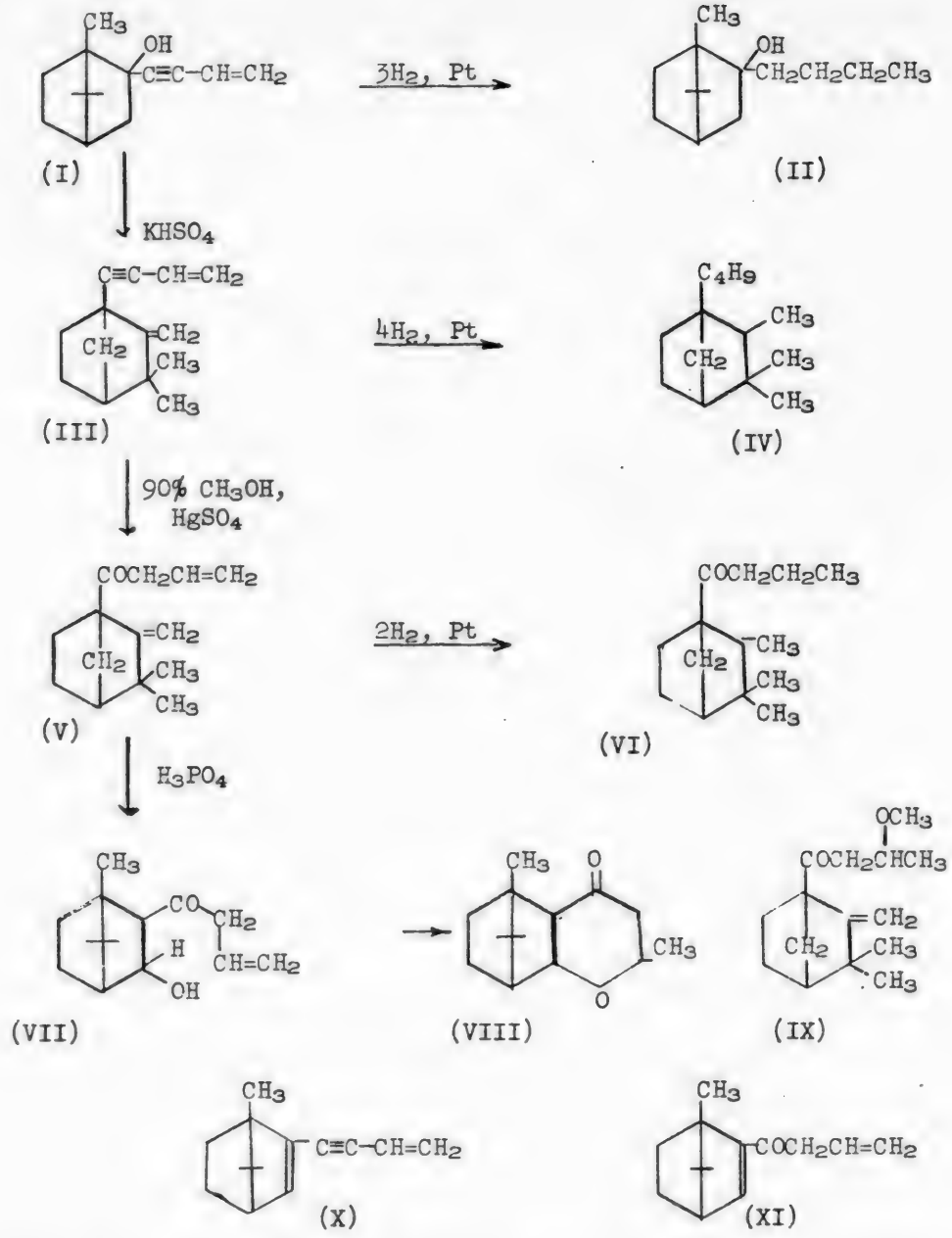


(R = H or CH_3)

The discovery of steric hindrance in the cyclization of allyl-Δ^1-cyclopentenyl ketones presents great theoretical interest and demonstrates the difficulty of formation of polycyclic systems with condensed five-membered rings. It also reveals the existence of a special and still unclarified stereochemical structure. These facts also readily account for the negative results obtained by Marvel in attempting the cyclohydration of di-Δ^1-cyclopentenylacetylene [5].

In the present paper we report a study of the behavior in the above-described transformations of vinylethynyl borneol (I), which we synthesized in 62% yield by the action of magnesium bromovinylacetylene on camphor. In the hydrogenation of vinylethynyl borneol (I) in presence of Pt catalyst, the theoretically required 3 molecules of hydrogen are absorbed and butylborneol (II) is formed. Dehydration of vinylethynyl borneol (I) is readily effected by heating with potassium bisulfate with formation in 70% yield of a dieneyne hydrocarbon, presumably vinylethynyl camphene (III), by the usual camphenic rearrangement during the dehydration of vinylethynyl borneol (I). Hydrogenation of the dieneyne (III) with Pt catalyst results in the absorption of 4 molecules of hydrogen, and a saturated hydrocarbon is formed to which we ascribe the structure of butyldihydrocamphene (IV).

Like other dieneynes, vinylethynyl camphene (III) is readily hydrated when heated in aqueous solutions of methanol in presence of mercuric sulfate, forming allylcamphenyl ketone (V) in about 80% yield. The latter absorbs 2 molecules of hydrogen on hydrogenation with Pt catalyst and forms propyldihydrocamphenyl ketone (VI). Under the conditions of hydration of the dieneyne (III) to allylcamphenyl ketone (V), one molecule of methanol becomes attached at the allyl group, yielding β-methoxypropylcamphenyl ketone (IX), distillation of which in vacuum in presence of p-toluene sulfonic acid leads to reversal of the process with re-formation of allylcamphenyl ketone (V). All our attempts to convert the dieneone (V) into a cyclic ketone were unsuccessful. When heated with phosphoric acid, the dieneone (V), likewise the carbinol (I) and the dieneyne (III), resinified completely, while treatment with phosphoric acid in the cold of allylcamphenyl ketone (V) caused hydration to a crystalline saturated compound with the formula $C_{14}H_{22}O_2$ to which we ascribe a pyrone structure (VIII). The latter



was most probably formed by hydration of the dieneone (V) with rearrangement of the carbon framework followed by cyclization of the resultant intermediate keto alcohol (VII). The pyrone (VIII) could have also been formed by hydration of vinylethynyl bornylene (X) and the corresponding dieneone (XI), but this route is not very probable since the dehydration of vinylethynyl borneol (I) must yield not vinylethynyl bornylene (X) but vinylethynyl camphene (III).

EXPERIMENTAL

Synthesis of 2-Vinylethynyl Borneol

A solution of 92 g camphor in 100 ml absolute ether was added in the course of 1 hour to an ethereal solution of magnesium vinylacetylene bromide prepared

from 21.6 g magnesium, 108 g ethyl bromide, 65 g vinylacetylene and 225 ml absolute ether. The reaction mixture was then stirred at 10-15° for 3 hours and left overnight. On the following day stirring was continued for another hour at room temperature and for $5\frac{1}{2}$ hours at the temperature of boiling ether. The cooled mixture was hydrolyzed with 10% hydrochloric acid (360 ml), the product extracted with ether, the solution neutralized with soda, dried with sodium sulfate, and fractionated in vacuum, yielding 78.5 g of 2-vinylethynyl borneol (I) in the form of a highly viscous, colorless liquid which crystallized in the receiver:

B.p. 89-90.5° at 2 mm; m.p. 37-37.5°.

4.540 mg substance: 13.700 mg CO_2; 4.050 mg H_2O.
Found %: C 82.35; H 9.98.
$C_{14}H_{20}O$. Computed %: C 82.25; H 9.87.

Hydrogenation of 2-Vinylethynyl Borneol

10 g substance in 45 ml ethyl alcohol was hydrogenated in presence of Pt catalyst. Hydrogenation was complete after 30 hours when 3.32 liters (3 molecules) of hydrogen had been absorbed. Distillation in vacuum of the hydrogenation product gave 8 g 2-butylborneol (II) in the form of a viscous, colorless liquid:

B.p. 93-94° at 3 mm; n_D^{20} 1.4832; d_4^{20} 0.9416; MR found 63.80; computed 63.97.

13.15 mg substance: 38.53 mg CO_2, 14.24 mg H_2O.
9.98 mg substance: 29.24 mg CO_2; 10.99 mg H_2O.
Found %: C 79.96, 79.95, H 12.12, 12.39.
$C_{14}H_{26}O$. Computed %: C 79.92, H 12.47.

Dehydration of 2-Vinylethynyl Borneol

A mixture of 78 g substance and 25 g freshly calcined finely pulverized potassium bisulfate was placed in a distillation flask provided with a dephlegmator, and heated in a nitrogen stream in the vacuum of a water-jet pump (8 mm); when the temperature of the bath reached 115°, distillation commenced. The distillate, b.p. 87-103° at 8 mm, was dried with calcium chloride and distilled in vacuum, yielding 50 g vinylethynyl camphene (III) in the form of a mobile, colorless liquid:

B.p. 99° at 7.5 mm; n_D^{20} 1.5340, d_4^{20} 0.9336;
MR found 61.98, computed 59.51.

4.565 mg substance: 15.067 mg CO_2, 3.930 mg H_2O.
Found %: C 90.07, H 9.63.
$C_{14}H_{18}$. Computed %: C 90.25, H 9.75.

Hydrogenation of Vinylethynyl Camphene

3 g substance in 15 ml glacial acetic acid was hydrogenated in presence of Pt catalyst. Hydrogenation was complete after 12 hours when 1.4 liters (4 molecules) of hydrogen had been absorbed. The product was neutralized with caustic alkali solution, extracted with ether, dried with sodium sulfate, and fractionated. There was obtained 2 g of butyldihydrocamphene (IV) in the form of a mobile, colorless liquid:

B.p. 94-95.5° at 10 mm; n_D^{20} 1.4705; d_4^{20} 0 8705, MR found 62.31; computed 62.45.

14.50 mg substance: 45.80 mg CO_2; 16.80 mg H_2O.
10.72 mg substance: 33.83 mg CO_2, 12.55 mg H_2O.

Found %: C 86.20, 86.12; H 12.96, 13.00.
$C_{14}H_{26}$. Computed %: C 86.51; H 13.50.

Hydration of Vinylethynyl Camphene

A mixture of 300 g of 95% methanol, 1 ml of concentrated sulfuric acid, 15 g mercuric sulfate (added in equal portions during the whole of the experiment) and 50 g dieneyne (III) was stirred for 9 hours at 60-65°. Following the heating, the methanol was distilled off in a low vacuum on the water bath (60°) in the course of 30 minutes. The residue was diluted with ether and neutralized with soda solution. The ether extract was dried with sodium sulfate and fractionated to give 47 g β-methoxypropylcamphenyl ketone (IX) in the form of a mobile, pale-yellow liquid:

B.p. 122-125° at 3 mm; n_D^{20} 1.4918; d_4^{20} 0.9981; MR found 68.58; computed 68.25.

17.96 mg substance: 48.90 mg CO_2; 16.32 mg H_2O.
10.14 mg substance: 27.64 mg CO_2; 9.33 mg H_2O.
Found %: C 74.31, 74.40; H 10.20, 10.29.
$C_{15}H_{24}O_2$. Computed %: C 76.25; H 10.24.

Removal of Methanol from the Methoxy Ketone (IX)

A mixture of 6.5 g substance and 0.03 g p-toluene sulfonic acid was heated in vacuum (170 mm) at 125-135° for 30 minutes. The cooled reaction product was extracted with ether, neutralized with soda solution, dried with sodium sulfate, and fractionated. There was obtained 4.5 g allylcamphenyl ketone (V) in the form of a pale-yellow, mobile liquid:

B.p. 104-106° at 3 mm; n_D^{20} 1.5068; d_4^{20} 0.9875; MR found 61.50; computed 61.53.

7.440 mg substance: 21.830 mg CO_2; 6.759 mg H_2O.
Found %: C 80.07; H 10.16.
$C_{14}H_{20}O$. Computed %: C 82.25; H 9.87.

Hydrogenation of Allylcamphenyl Ketone

2.75 g substance in 15 ml glacial acetic acid was hydrogenated in presence of Pt catalyst. Hydrogenation was complete after 20 hours when 600 ml (2 molecules) of hydrogen had been absorbed. The product was neutralized with caustic alkali solution, extracted with ether, dried with sodium sulfate, and distilled. There was obtained 1.5 g of propyldihydrocamphenyl ketone (VI) in the form of a colorless, mobile liquid:

B.p. 105-106° at 3.5 mm; n_D^{20} 1.4805; d_4^{20} 0.9679; MR found 61.17. computed 62.46.

3.818 mg substance: 11.234 mg CO_2; 3.739 mg H_2O.
3.650 mg substance: 10.754 mg CO_2; 3.640 mg H_2O.
Found %: C 80.26, 80.37; H 10.94, 11.16.
$C_{14}H_{24}O$. Computed %: C 80.70; H 11.62.

Crystalline derivatives of this ketone could not be obtained.

Ozonation of Allylcamphenyl Ketone

Ozonized oxygen (6% ozone) was passed at the rate of 4.5 liters/hour for 12 hours through a solution of 4 g substance in 35 ml dry chloroform. The chloroform solution of the ozonide was poured into water (35 ml) and the mixture stirred for 3 hours at room temperature. On the following day 30% hydrogen peroxide was added and stirring continued for 8 hours at 55-60°. The product was

neutralized with soda (3.2 g), the chloroform layer separated, and the aqueous layer extracted with ether. After the solutions had been dried with sodium sulfate, the ether and chloroform were driven off on the water bath, but the residue of neutral products was insignificant (0.2 g). Analysis of the aqueous solution of salts by the calomel method gave 0.4654 g formic acid (69% of theory). The solution was evaporated to dryness in vacuum, the residue acidified with concentrated hydrochloric acid (7 ml) and extracted with ether. The ether extract of the organic acids was dried with sodium sulfate and fractionated. There were obtained 0.35 g formic acid (b.p. 99.5-101° at 750 mm) and 2.25 g of an organic acid in the form of a viscous, transparent, pale-yellow oil which it was impossible to crystallize.

Hydration of Allylcamphenyl Ketone

A mixture of 15 g dieneone (V) and 15 ml phosphoric acid (sp. gr. 1.78) was stirred at room temperature for 10 hours. The reaction product was dissolved in ether, neutralized with soda solution, dried with sodium sulfate, and fractionated in vacuum. There was obtained 6.3 g of a colorless, very viscous liquid:

B.p. 121-123° at 3 mm; n_D^{20} 1.5020,

partially crystallizing on standing. 2.5 g of crystals of tetrahydro-γ-pyrone (VIII) was filtered off, m.p. 94.5-96° (from petroleum ether).

7.670 mg substance: 21.307 mg CO_2, 6.930 mg H_2O.
5.780 mg substance. 16.057 mg CO_2, 5.270 mg H_2O.
Found %. C 75.81, 75.81; H 10.10, 10.20.
$C_{14}H_{22}O_2$. Computed %. C 75.68; H 9.93.

0.1208 g substance: 15.80 g benzene. Δt 0.17°.
0.4940 g substance: 15.78 g benzene. Δt 0.70°.
Found: M 229, 230.
Computed: M 222.

It was impossible to prepare crystalline derivatives of the pyrone (VIII). On shaking a solution of pyrone (VIII) in glacial acetic acid in a hydrogen atmosphere over Pt catalyst, no hydrogen was taken up and the compound was recovered unchanged.

SUMMARY

1. Reaction of magnesium vinylacetylene bromide with camphor gave a 62% yield of 2-vinylethynyl borneol (I) which underwent dehydration on distillation in vacuum over potassium bisulfate to form 2-vinylethynyl camphene (III) in a yield of 70%.

2. Hydration of the dieneyne (III) in aqueous methanol in presence of mercuric sulfate gave allylcamphenyl ketone (V) which adds on one molecule of methanol and gives β-methoxypropylcamphenyl ketone (IX). Cleavage of methanol from the methoxy ketone (IX) gave allylcamphenyl ketone (V).

3. Allylcamphenyl ketone is completely incapable of cyclization and on treatment with phosphoric acid is only hydrated to a saturated compound $C_{14}H_{22}O_2$ to which is ascribed the structure of the tetrahydro-γ-pyrone (VIII).

4. The unsaturated compounds (I, III, and IV) were hydrogenated with Pt catalyst to the corresponding saturated compounds (II, IV, and VI).

LITERATURE CITED

[1] I.N.Nazarov and coworkers, Bull. Acad. Sci. USSR, Div. Chem. Sci., 211 (1941); 200 (1942); 65 (1944), 529, 633 (1946); 51, 205, 277, 353 (1947). J. Gen.

Chem. 18, 665, 675, 681, 896, 911, 1077, 1083 (1948).

[2] I.N.Nazarov and co-workers, J.Gen.Chem. 19, 1870 (1949); 20, 1441, 1449 (1950).*

[3] I.N.Nazarov and L.N.Pinkina, J.Gen.Chem. 20, 2009 (1950).**

[4] I.N.Nazarov and M.S.Burmistrova, Bull. Acad. Sci. USSR, Div. Chem. Sci., 51 (1947).

[5] Pinkney and Marvel, J.Am.Chem.Soc., 59, 2669 (1937).

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*See CB translation p. a-331 ff., 1501 ff, 1509 ff.,

**See CB translation p. 2079 ff.

ACETYLENE DERIVATIVES

123. HYDRATION OF ISOPROPYLVINYLETHYNYL CARBINOL TO 2-METHYL-5-ISOPROPYL-TETRAHYDRO-4-FURANONE AND 2-ISOPROPYLTETRAHYDRO-4-PYRONE

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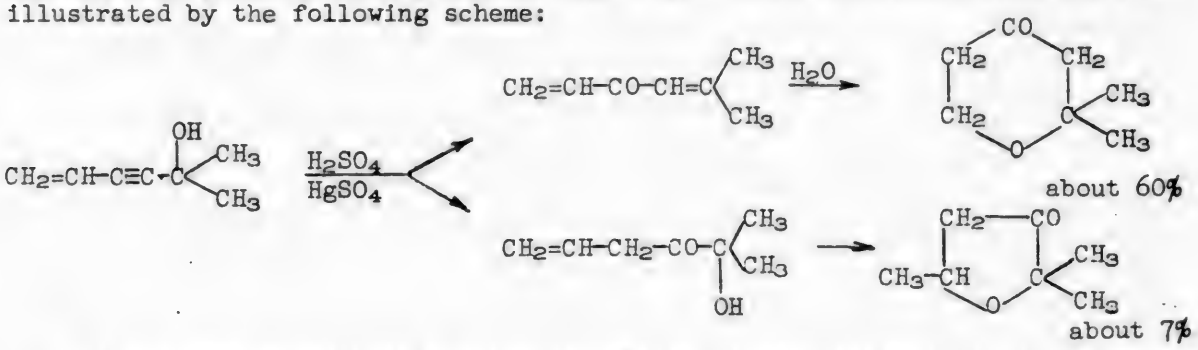
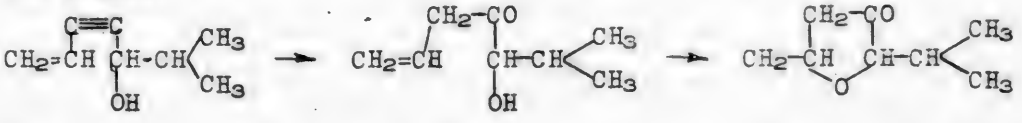
In one of the earlier communications from our laboratory it was shown [1] that dimethylvinylethynyl carbinol is transformed in two directions when heated with dilute sulfuric acid in presence of mercuric sulfate. By far the greater proportion of the carbinol isomerizes to β,β-dimethyldivinyl ketone, which undergoes hydration to 2,2-dimethyltetrahydro-4-pyrone. The latter is isolated in a yield of about 60%. A small amount of the carbinol undergoes direct hydration to an intermediate unsaturated keto alcohol (5-methyl-1-hexen-5-ol-4-one) which cyclizes to 2,5,5-trimethyltetrahydro-4-furanone. The latter is isolated from the reaction products in a yield of only 7-8%. These transformations may be illustrated by the following scheme:

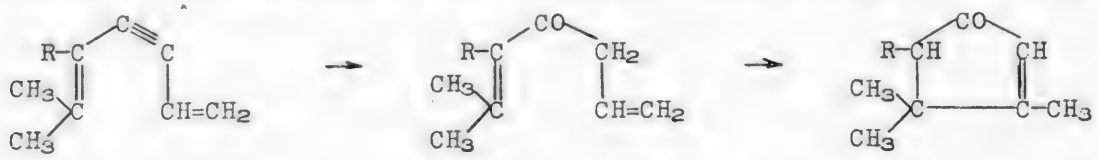


It was here found that the transformation of vinylethynyl carbinols into the corresponding furanones may constitute the chief and even the sole course of the reaction. This behavior is more conspicuously exhibited by isopropylvinylethynyl carbinol, which when heated with phosphoric acid gives a single reaction product in the shape of 2-methyl-5-isopropyltetrahydro-4-furanone in a yield of up to 40%. The mechanism of this reaction, as already shown [1], involves the direct hydration of the triple bond of the carbinol to an unsaturated α-keto alcohol and cyclization of the latter to the furanone in accordance with the scheme:



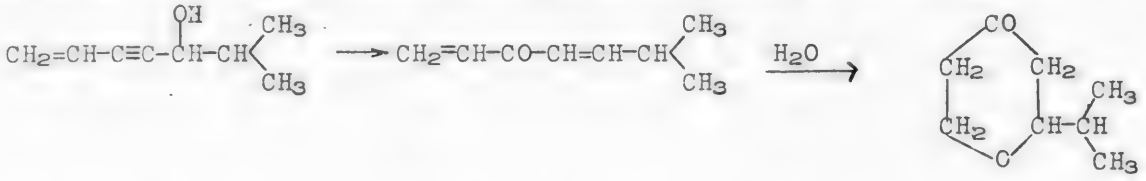
The characteristic behavior of isopropylvinylethynyl carbinol toward phosphoric acid is undoubtedly bound up with the difficulty of its dehydration to

6-methyl-1,5-heptadien-3-yne, in consequence of which the reaction is exclusively directed toward the hydration of the triple bond of the carbinol. We were unable to effect the dehydration of isopropylvinylethynyl carbinol even with the aid of potassium bisulfate, p-toluene sulfonic acid or sulfuric acid. Our interest in the dehydration of isopropylvinylethynyl carbinol derives from the fact that we were attempting to prepare 6-methyl-1,5-heptadien-3-yne by this route in order to study the mechanism of its hydration and cyclization. The latter reactions should lead to 2,2,3-trimethyl-Δ^2- cyclopenten-5-one, in analogy with the transformations of the homologs of this simplest 1,1-disubstituted dieneyne, [2]:



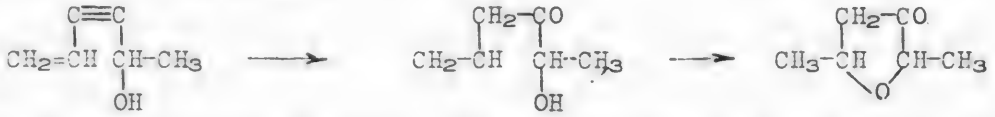
R = CH_3, $(CH_3)_2CH$, $(CH_3)_3C$, C_6H_5

Isopropylvinylethynyl carbinol behaves analogously to other vinylethynyl carbinols [3] when heated with dilute sulfuric acid in acetone solution in presence of mercuric sulfate, and is converted in about 50% yield into 2-isopropyltetrahydro-4-pyrone. This transformation involves preliminary isomerization of the isopropylvinylethynyl carbinol to β-isopropyldivinyl ketone and dehydration of the latter to 2-isopropyltetrahydro-4-pyrone according to the scheme:



Depending therefore upon the reaction conditions, isopropylvinylethynyl carbinol may undergo transformation either by way of its direct hydration to 2-methyl-5-isopropyltetrahydro-4-furanone or by way of preliminary isomerization to β-isopropyldivinyl ketone followed by hydration of the latter to 2-isopropyltetrahydro-4-pyrone.

It might have been expected on the basis of the behavior of isopropylvinylethynyl carbinol in presence of phosphoric acid, that other secondary vinylethynyl carbinols would also be readily transformed into the corresponding furanones. Accordingly we investigated the behavior toward phosphoric acid of methylvinylethynyl carbinol in the expectation of preparing 2,5-dimethyltetrahydro-4-furanone according to the scheme:



We failed, however, to effect this transformation because methylvinylethynyl carbinol completely resinified when heated with concentrated phosphoric acid (sp. gr. 1.75 and higher), while when heated with dilute phosphoric acid (sp. gr. 1.7 and lower) it was recovered unchanged.

EXPERIMENTAL

Synthesis of Isopropylvinylethynyl Carbinol

To vinylacetylene-magnesium bromide prepared in the usual manner (from 13.2 g magnesium, 66 g ethyl bromide, 150 ml absolute ether, and 55 g gaseous vinyl-

acetylene) was added 35 g isobutyric aldehyde in 35 ml absolute ether in the course of 30 minutes through a dropping funnel at room temperature.

The reaction mixture was heated for 4 hours at the boiling point of ether, and was left overnight. After working up and distillation in the usual manner, 50 g of isopropylvinylethynyl carbinol was isolated:

B.p. 78-81° at 18 mm; n_D^{20} 1.4770 [4].

Yield 83%.

Hydration of Isopropylvinylethynyl Carbinol to 2-Methyl-5-isopropyltetrahydro-4-furanone

15 g Isopropylvinylethynyl carbinol and 15 ml phosphoric acid (sp. gr. 1.76) were heated with vigorous stirring for 6 hours at 60-65°. The reaction product was diluted with water, neutralized with soda, extracted with ether, dried, and fractionated in vacuum. There was obtained 5.5 g of 2-methyl-5-isopropyltetrahydro-4-furanone in the form of a mobile, colorless liquid with a pleasant odor:

B.p. 170-173° at 760 mm; 68-70° at 16 mm; n_D^{20} 1.4440; d_4^{20} 0.9604; MR found 39.27; computed 38.60.

5.165 mg substance: 12.898 mg CO_2; 4.650 mg H_2O.
6.210 mg substance: 15.429 mg CO_2; 5.510 mg H_2O.
Found %: C 67.85, 67.81; H 10.07, 9.96.
$C_8H_{14}O_2$. Computed %: C 67.60; H 9.86.

In addition to the furanone described above, this experiment also yielded 7 g of undistillable resin. 2-Methyl-5-isopropyltetrahydro-4-furanone readily forms a semicarbazone which after recrystallization from ethanol melts at 200°:

4.227 mg substance: 0.785 ml N_2 (19°, 752 mm).
4.320 mg substance: 0.807 ml N_2 (20°, 751 mm).
Found %: N 21.48, 21.50.
$C_9H_{17}O_2N_3$. Computed %: N 21.10.

The carbinol is recovered unchanged when isopropylvinylethynyl carbinol is stirred with phosphoric acid (sp. gr. 1.76) for 72 hours at room temperature; a mixture of the carbinol and the furanone is obtained when the carbinol is heated with the same acid for 15 hours at 40-50°. The original material is recovered unchanged when the carbinol is heated with potassium bisulfate at 150° in a 150 mm vacuum for 30-40 minutes. Resinification occurs when the carbinol is heated with p-toluene sulfonic acid in a nitrogen stream at 100° in vacuum for only 20 minutes.

Hydration of Isopropylvinylethynyl Carbinol to 2-Isopropyltetrahydro-4-pyrone

11.5 g of isopropylvinylethynyl carbinol, 60 mg acetone, 24 ml 10% sulfuric acid and 1.2 g mercuric sulfate were refluxed for 20 hours with energetic stirring. The mercuric sulfate was introduced in small portions at intervals of 4-5 hours. The product was worked up in the usual manner and distilled in vacuum to give 6 g 2-isopropyltetrahydro-4-pyrone in the form of a colorless liquid with a specific pleasant odor:

B.p. 193-194° at 760 mm; n_D^{20} 1.4495; d_4^{20} 0.9822; MR found 38.81; computed 38.60.

5.385 mg substance: 13.300 mg CO_2; 4.891 mg H_2O.
7.069 mg substance: 17.425 mg CO_2; 6.331 mg H_2O.
Found %: C 67.40, 67.25; H 10.16, 10.01.
$C_8H_{14}O_2$. Computed %: C 67.60; H 9.86.

2-Isopropyltetrahydro-4-pyrone readily forms a semicarbazone which after recrystallization from ethanol melts at 165°:

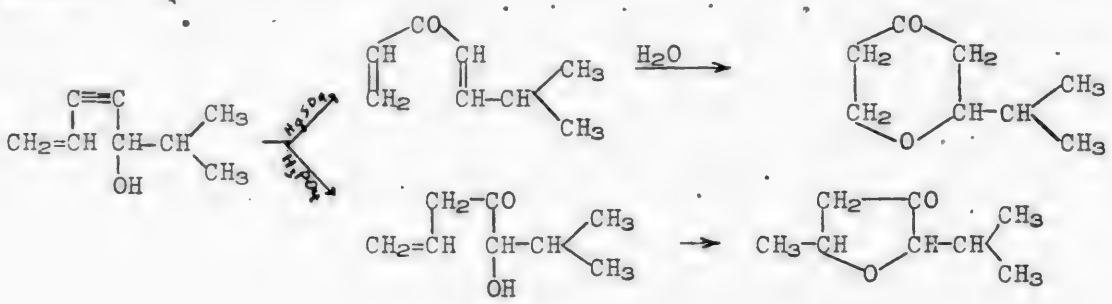
4.745 mg substance: 0.865 ml N_2 (21°, 751 mm).
4.725 mg substance: 0.897 ml N_2 (21°, 730 mm).
Found %: N 20.96, 21.17.
$C_9H_{17}O_2N_3$. Computed %: N 21.10.

Comparative Table of Physical Properties of 2-Methyl-5-isopropyltetrahydro-4-furanone and 2-Isopropyltetrahydro-4-pyrone

Name	B.p. at 760 mm	n_D^{20}	d_4^{20}	MR found	MR computed	M.p. of semicarbazone
2-Methyl-5-isopropyltetrahydro-4-furanone	170-173°	1.4440	0.9604	39.27	28.60	200°
2-Isopropyltetrahydro-4-pyrone.....	193-194	1.4495	0.9822	38.87	38.60	165

SUMMARY

2-Methyl-5-isopropyltetrahydro-4-furanone and 2-isopropyltetrahydro-4-pyrone have been obtained by the hydration of isopropylvinylethynyl carbinol. A mechanism for these transformations is given which is illustrated by the following scheme:



LITERATURE CITED

[1] I.N.Nazarov and I.V.Torgov, J.Gen.Chem. 18, 1332 (1948).

[2] I.N.Nazarov and coworkers, J.Gen.Chem. 19, 1870 (1949); 20, 1441, 1449 (1950).*

[3] I.N.Nazarov and coworkers, Bull. Acad. Sci. USSR, Div. Chem. Sci., 223 (1940); 50 (1943); 495, 647 (1947).

[4] I.N.Nazarov and A.N.Elizarova, Bull. Acad. Sci. USSR, Div. Chem. Sci., 189 (1940); Carothers and Berchet, J.Am.Chem.Soc., 55, 1094 (1933).

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*See CB translation p. a-331 ff., 1501 ff., 1509 ff.

ACETYLENE DERIVATIVES

124. α-KETOXIDES AND THEIR TRANSFORMATIONS

I. THE OXIDATION OF MESITYL OXIDE AND OF 1-METHOXY-5-METHYL-4-HEXEN-3-ONE TO THE CORRESPONDING α-KETOXIDES

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The oxidation of various types of olefinic compounds to the corresponding α-oxides or glycols is the subject of an extensive literature.

As far back as 1909, Prilezhaev [1] discovered a general method for the preparation of α-oxides by the action of benzoyl hydroperoxide on olefins in a medium of an inert solvent. A variety of α-glycols is also readily obtained by the action of hydrogen peroxide on olefins. This reaction is effected either in solution in tertiary alcohols (butyl and amyl) in presence of catalysts (OsO_4, V_2O_3, CrO_3 [2]) or in solution in anhydrous formic [3] or acetic [4] acid. In addition to olefinic hydrocarbons, unsaturated alcohols, acids, ethers, halogen derivatives and ketones with an isolated double bond may also be hydroxylated by this method. However, α,β-unsaturated ketones are not readily amenable to oxidation and hydroxylation in this way, the reaction generally being accompanied by rupture of the double bond.

Although in some cases it is also possible by the other methods to convert α,β-unsaturated ketones into the corresponding keto glycols in small yield, it has been found quite impossible to apply such methods to the conversion of α,β-unsaturated ketones into the corresponding α-ketoxides.

The first representative of the α-ketoxides was prepared in 1913 by Widmann [5] who condensed benzaldehyde with bromacetophenone in presence of sodium ethylate:

$$C_6H_5CHO + BrCH_2COC_6H_5 \xrightarrow{C_2H_5ONa} C_6H_5CH\!-\!O\!-\!CHCOC_6H_5$$

According to Jörlander [6], this method is only applicable to the preparation of aromatic oxides, but Timnikova and Martynov [7] also used it to obtain good yields of ketoxides of the aliphatic-aromatic series.

In 1921 Weitz and Scheffer [8] described a simple method for the preparation of α-ketoxides by the action of alkali peroxides on α,β-unsaturated ketones:

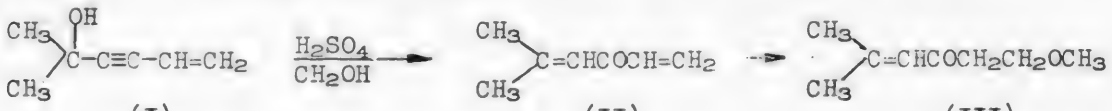
$$>C{=}C(\text{-})CO- \xrightarrow[\text{alkali}]{H_2O_2} >C\!-\!O\!-\!C(\text{-})CO-$$

Up to now, however, this method has been used principally for aromatic ketones.

In our laboratory about 10 years ago simple methods were developed, on the basis of isomerization of vinylethynyl carbinols in presence of mercury salts, for the preparation of the most diverse of α,β-unsaturated alkoxy ketones and divinyl ketones, which have already been the object of systematic investigations for many years.

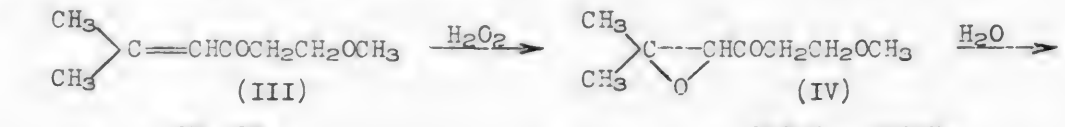
It was considered of interest to utilize these readily accessible divinyl ketones and α,β-unsaturated alkoxy ketones for the study of their oxidation reactions with the aim of preparing the corresponding α-ketoxides, ketodioxides, keto glycols, and keto erythritols, which are potentially important starting materials for new and interesting compounds, including some which border on the carbohydrates.

The first compound selected for this investigation was 1-methoxy-5-methyl-4-hexen-3-one (III) which is easily prepared, as previously shown [9], by isomerization of dimethylvinylethynyl carbinol (I) in methanol solution:



(I) (II) (III)

The expected oxidation of the double bond takes place smoothly when the methoxy ketone (III) is oxidized with alkaline hydrogen peroxide, and the ketoxide (IV) is formed in a yield of about 70%. On heating with water the latter compoun is hydroylzed to the keto glycol (V), which by means of acetic anhydride is converted into its diacetate (VI):

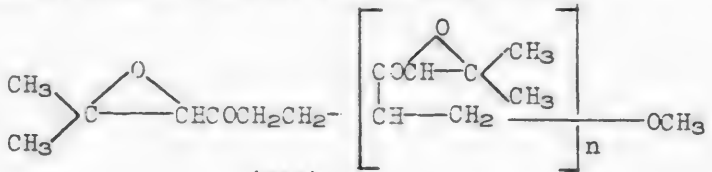


(III) (IV) (V) (VI)

Treatment of the methoxy ketone (III) with alkaline hydrogen peroxide yields, in addition to the ketoxide (IV), a substance, $C_8H_{16}O_4$ of unidentified structure in a yield of about 20%. It is isomeric with the keto glycol (V) but differs markedly in its much lower boiling point and in containing only one hydroxyl group.

Distillation of the ketoxide (IV) with p-toluenesulfonic acid in vacuum does not result in methanol being split off, isomerization apparently taking place with formation in about 50% yield of a product of unidentified structure with constants similar to those of the initial ketoxide.

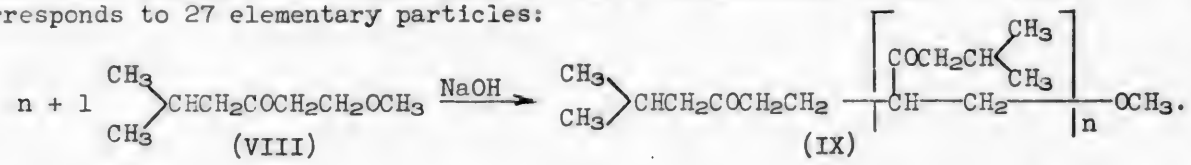
In presence of alkali, the ketoxide (IV) readily undergoes condensation to a solid polymer with loss of methanol at the expense of the methoxy group and the hydrogen of the methylene group adjacent to the carbonyl group. The mean molecular weight of this polymer corresponds to ten elementary particles and its structure is represented by the formula (VII):



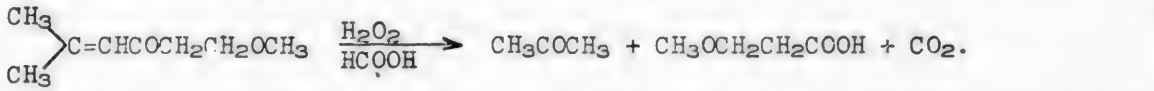
(VII)

No trace of the ketoxide(IV) could be isolated when the methoxy ketone (III) was oxidized with alkaline hydrogen peroxide in acetone solution, since under these conditions it is completely condensed to the polymer (VIII), as was demonstrated in a special experiment.

A similar behavior toward alkalies is exhibited by 1-methoxy-5-methylhexane-3-one (VIII), which under the influence of alkali likewise condenses (but rather more slowly) to a liquid polymer (IX), the molecular weight of which corresponds to 27 elementary particles:



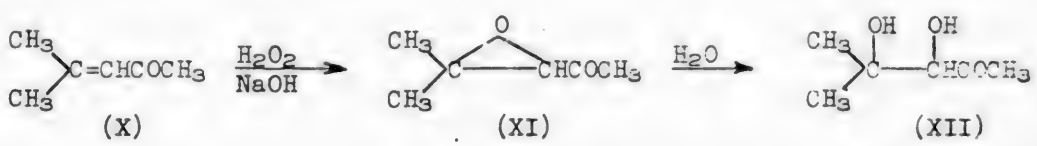
The keto glycol (V) was also prepared in small yield by addition of hydrogen peroxide to the methoxy ketone (III) dissolved in tertiary butyl alcohol in presence of osmium tetroxide [2]. On the other hand, reaction of hydrogen peroxide with the methoxy ketone (III) in anhydrous formic acid [3] results in almost complete cleavage of the double bond with formation of acetone and β-methoxypropionic acid in a yield of 75-80%:



The smooth course of this reaction may be exploited for synthetic purposes in the preparation of β-alkoxypropionic acids as well as for the determination of the structure of related compounds, in place of ozonation.

The reaction of acetyl hydroperoxide with the methoxy ketone (III) in solution in glacial acetic acid solution leads to partial cleavage of the molecule with formation of β-methoxypropionic acid in a yield of about 30%. Concurrently the double bond of the methoxy ketone (III) is oxidized, resulting in the formation in a total yield of 30-35% of neutral products, the main component of which is a crystalline substance of unidentified structure with the composition $C_{13}H_{24}O_6$. The ketoxide (IV) may also be among the neutral products, but it could not be isolated in the pure form.

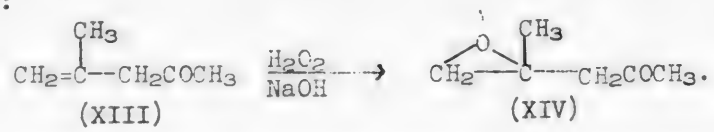
Thus, the method using alkaline hydrogen peroxide gives the smoothest oxidation of the unsaturated methoxy ketone (III), with retention of the carbon skeleton, of all of the methods tested. For the purpose of comparison, this method was also tried out with mesityl oxide. Treatment of mesityl oxide (X) with alkaline hydrogen peroxide yielded the previously described [8] ketoxide (IX) in small yield; its hydrolysis with water gave the keto glycol (XII) which has also been previously prepared by the hydroxylation of mesityl oxide [10]:



The reaction of mesityl oxide with hydrogen peroxide differs from that with the methoxy ketone (III) in being extremely complicated and leading to the formation of two isomeric ketoxides (XI), in addition to low-boiling products of decomposition and high-boiling products from which was isolated a substance, $C_8H_{12}O_3$, isomeric with the keto glycol (XII), but with a much lower boiling point.

The second high-boiling isomer was possibly formed by oxidation of the iso

modification [11] of mesityl oxide, so that it may have the structure represented by formula (XIV):



(XIII) (XIV)

EXPERIMENTAL

1-Methoxy-5-methyl-4-hexen-3-one (II) was prepared, as already described [9], by the isomerization of dimethylvinylethynyl carbinol in methanol solution in presence of mercuric sulfate. It has the constants:

B.p. 91° at 18 mm, n_D^{20} 1.4550.

Mesityl oxide was distilled before the experiment and had b.p. 129-131° and n_D^{20} 1.4435.

Oxidation of 1-Methoxy-5-methyl-4-hexen-3-one with Alkaline Hydrogen Peroxide. Preparation of the Ketoxide (IV)

In a three-necked flask provided with a mechanical stirrer, a thermometer, and two dropping funnels was placed a solution of 155 g methoxy ketone (III) in 1000 ml methanol; the solution was cooled with an ice-salt mixture (-10°) and with continuous stirring 268 ml 15% hydrogen peroxide (1 mole) and 37 ml 4 N aqueous solution of sodium hydroxide were run in simultaneously over a period of two hours. The oxidation is strongly exothermic. The rate of addition of the hydrogen peroxide and alkali was so regulated that the temperature of the liquid did not exceed 0°. The hydrogen peroxide remaining in the reaction mixture was analyzed by titrating samples with sodium hyposulfite. 11.54 g of hydrogen peroxide was found in the reaction mixture 30 minutes after addition of the reagents (out of a total of 40.2 g). After 40 minutes there remained 4.47 g, and after 1 hour 20 minutes substantially the whole of the hydrogen peroxide had entered into reaction.

The solution was neutralized with 10% sulfuric acid (45 ml), the separated sodium sulfate was filtered off, the methanol driven off in a low vacuum, and the reaction product extracted with ether, dried with magnesium sulfate, and fractionated in vacuum.

There was obtained 100 g of ketoxide (IV) in the form of a colorless, mobile liquid with a faint characteristic odor:

B.p. 73-74° at 2.5 mm; n_D^{20} 1.4389; d_4^{20} 1.0135; MR found 40.96; computed 40.24, (increment of the oxide ring 0.7).

6.354 mg substance. 14.125 mg CO_2; 5.115 mg H_2O.
3.567 mg substance. 7.925 mg CO_2; 2.889 mg H_2O.
Found %: C 60.67, 60.63; H 9.01, 9.06.
$C_8H_{14}O_3$. Computed %. C 60.75; H 8.86.

0.4095 g substance: 16.0 g benzene. Δt 0.805°.
0.4916 g substance: 16.0 g benzene: Δt 0.987°.
Found. M 164, 161.
$C_8H_{14}O_3$. Computed: M 158.

The ketoxide (IV) is soluble in water and in the usual solvents; in contact with the skin it causes itching and develops blisters.

The semicarbazone of the α-ketoxide (IV) melts at 87-88°, but it could not be recrystallized since it does not separate from solution even after complete evaporation of the solvents (methanol, ethanol).

The oxide oxygen of the ketoxide (IV) was determined by the method of Nicolet and Poulter [12]. A weighed amount of substance was introduced into 0.2 N solution of dry hydrogen chloride in absolute ether. The solution was kept in a flask with a ground glass stopper at room temperature, and the excess hydrogen chloride was back-titrated with 0.1 N solution of alcoholic caustic alkali. In this manner it was found that the ketoxide reacts in 2 hours to the extent of 56.4%, in 17 hours 64.25%, and in 7 days 90.3%.

The data show that rupture of the oxide ring by hydrogen chloride proceeds slowly under these conditions, requiring over 7 days for its completion.

Apart from the ketoxide (IV) the above experiment yielded 34 g high-boiling products consisting mainly of a substance, $C_8H_{16}O_4$ [an isomer of the keto glycol (V)] with the following constants:

B.p. 76-78° at 2.5 mm; n_D^{20} 1.4455; d_4^{20} 1.0781; MR found 43.49; computed 43.85.

9.00 mg substance: 18.08 mg CO_2; 7.20 ml H_2O.
7.80 mg substance: 15.63 mg CO_2; 6.16 mg H_2O.
Found %: C 54.80, 54.68; H 8.95, 8.89.
$C_8H_{16}O_4$. Computed %: C 54.54; H 9.09.

Hydroxyl group determination by the method of Chugaev and Tserevitinov:

0.1860 g substance: 20.2 ml CH_4 (17.5°, 752.5 mm).
0.0593 g substance: 6.14 ml CH_4 (17.5°, 752.5 mm).
Found %: OH 7.71, 7.90.
$C_8H_{15}O_3(OH)$. Computed %: OH 9.61.

Hydrolysis of the Ketoxide (IV). Preparation of 1-Methoxy-5-methylhexan-4,5-diol-3-one (V)

A solution of 30 g ketoxide (IV) in 250 ml distilled water was heated on the water bath at 70-72° for 14 hours. The color of the solution changed to green and drops of an oily product settled to the bottom of the flask. The solution was filtered and evaporated to a syrup in vacuum. The distillate was dried with potassium carbonate, and extracted with ether, and the syrup was added to the ether extracts. After drying with anhydrous magnesium sulfate and driving off the ether, the residue was distilled in vacuum to give 12 g of unchanged ketoxide (IV) and 12 g of ketoglycol (V) in the form of a thick, colorless liquid devoid of odor:

B.p. 110° at 1.5 mm; n_D^{20} 1.4555; d_4^{20} 1.1025; MR found 43.354; computed 43.85.

16.08 mg substance: 32.05 mg CO_2; 12.98 mg H_2O.
11.58 mg substance: 23.71 mg CO_2; 9.43 mg H_2O.
Found %: C 54.39, 54.61; H 9.02, 9.06.
$C_8H_{16}O_4$. Computed %: C 54.54; H 9.09.

Determination of hydroxyl groups by the method of Chugaev and Tserevitinov:

0.04 g substance: 11.3 ml CH_4 (18.5°, 727.8 mm).
Found %: OH 19.35.
$C_8H_{14}O_2(OH)_2$. Computed %: OH 19.31.

The keto glycol (V) is readily soluble in water and the common organic solvents. It does not form a crystalline phenylosazone.

Preparation of the Acetate of 1-Methoxy-5-methylhexan-4,5-diol-3-one (VI)

10 g keto glycol (V) was dissolved in 50 g freshly distilled acetic anhydride, 5 g dry sodium acetate was added, and the mixture heated on the water bath at 70°

for 10 hours. The contents of the flask were poured in a thin stream into iced water (200 ml), the acetic acid was neutralized with soda, the product extracted with ether, and the extract dried with magnesium sulfate and fractionated in vacuum. Double distillation gave 6 g of the diacetate of the keto glycol (VI) in the form of a thick, colorless liquid devoid of odor:

B.p. 106-106.5° at 1 mm; n_D^{20} 1.4425; d_4^{20} 1.0978; MR found 62.726; computed 62.578.

5.588 mg substance: 11.331 mg CO_2, 3.909 mg H_2O.
6.897 mg substance: 14.052 mg CO_2; 4.877 mg H_2O.
Found %: C 55.34, 55.60; H 7.82, 7.85.
$C_{12}H_{20}O_6$. Computed %: C 55.39; H 7.69.

0.1202 g substance: 14.0 g benzene: Δt 0.200°.
0.1814 g substance: 14.0 g benzene: Δt 0.298°.
Found: M 222, 223.
$C_{12}H_{20}O_6$. Computed: M 260.

The compound does not contain free hydroxyl groups.

It was impossible to prepare the diacetate of the keto glycol (VI) directly from the ketoxide (IV) by the action of a mixture of acetic anhydride and glacial acetic acid in presence of sodium acetate.

Oxidation of 1-Methoxy-5-methyl-4-hexen-3-one (III) with Alkaline Hydrogen Peroxide in Dioxane. Preparation of a Polymer of the Ketoxide (VII)

Into a solution of 200 g methoxy ketone (III) in 1000 ml dioxane was poured, as described above, in the course of 1 hour 20 minutes, 328 ml 15% hydrogen peroxide (1 mole) and 40 ml 4 N aqueous solution of sodium hydroxide. Little heat was developed. After 30 minutes had elapsed from the addition of the reagents, the solution contained 40.8 g hydrogen peroxide (out of a total of 49.4 g added). A strong thermal effect was observed after the addition of an additional 40 ml of 4 N sodium hydroxide solution. The temperature of the solution rose to +14° (the temperature of the cooling bath was -16°). Within 1.5 hours after addition of the sodium hydroxide solution the hydrogen peroxide content of the reaction mixture had fallen to 7 g. On the following day the solution was neutralized with 10% sulfuric acid, the precipitated sulfate was filtered off, and the dioxane was removed in vacuum. The residue was a thick polymer which solidified after addition of water. After two reprecipitations with water from methanol solution and drying in a vacuum desiccator to constant weight, there was obtained 200 g of solid polymer (VII) in the form of a fine amorphous powder with a yellow color and m.p. 110-117°.

12.17 mg substance: 29.47 mg CO_2; 9.08 mg H_2O.
10.24 mg substance: 24 83 mg CO_2; 7.54 mg H_2O.
Found %. C 66.08, 66.19; H 8.35, 8.25.
$H[C_7H_{10}O_2]_{10}OCH_3$ Computed %: C 65.89; H 8.05.

11.400 mg substance: 2.09 ml 0.02 N solution $Na_2S_2O_3$.
12.501 mg substance: 2.30 ml 0.02 N solution $Na_2S_2O_3$.
Found %: OCH_3 1.90, 1.90.
$C_{70}H_{101}O_{20}(OCH_3)$. Computed%. OCH_3 2.39.

0.3941 g substance: 16.0 g benzene: Δt 0.108°.
0.6637 g substance: 16.0 g benzene: Δt 0.1625°.
Found: $M_{ave.}$ 1268, 1300.
$C_{71}H_{104}O_{21}$. Computed: M 1292.

The polymer (VII) was very readily soluble in methanol, acetone and ether,

less easily soluble in ethanol and benzene. It is precipitated from solutions by water and petroleum ether.

When the oxidation of the methoxy ketone (III) is carried out in an acetone medium, the polymer (VII) was likewise isolated as the sole product in quantitative yield.

Preparation of Polymer (VII) by Polymerization of the Ketoxide (IV)

To a solution of 18 g ketoxide (IV) in 100 ml dioxane was added 8 ml of 4 N solution of sodium hydroxide and 25 ml water. The temperature of the solution rose from 20 to 38° and the color changed to dark red. After cooling to room temperature, the solution was left overnight and on the following day the product was neutralized and isolated as previously described. There was obtained a solid polymer which after 3 reprecipitations with water from methanol solution had m.p. 120-125° and properties identical with those of the above-described polymer (VII).

Polymerization of 1-Methoxy-5-methylhexan-3-one (VIII).
Preparation of Polymer (IX)

1-Methoxy-5-methylhexan-3-one (VIII) was prepared by the catalytic hydrogenation of the methoxy ketone (III) in an autoclave in presence of Raney nickel, and had the following constants:

B.p. 70° at 10 mm; n_D^{18} 1.4208 [s].

To a solution of 40 g methoxy ketone (VIII) in 125 ml dioxane was added 19 ml 4 N sodium hydroxide solution and 40 ml ethanol. The solution was left at room temperature for 17 days and then worked up as described above.

There was obtained 32 g liquid polymer which did not distil in high vacuum. After two reprecipitations from methanol solution with water and prolonged drying in a vacuum desiccator over phosphorus pentoxide, a polymer (IX) was obtained in the form of a thick, transparent syrup with a cherry-red color.

15.82 mg substance: 43.52 mg CO_2; 14.81 mg H_2O.
11.05 mg substance: 30.26 mg CO_2; 10.62 mg H_2O.
6.811 mg substance: 0.78 ml 0.02 N solution $Na_2S_2O_3$.
8.112 mg substance: 0.73 ml 0.02 N solution $Na_2S_2O_3$.
Found %: C 74.90, 74.73; H 10.56, 10.75;
OCH_3 1.19, 0.94.
$H[C_7H_{12}O]_{27}OCH_3$. Computed %: C 74.93; H 10.73; OCH_3 1.01.

Direct determination of the molecular weight of polymer (IX) by the cryoscopic method gave a very low value (460 in the case of dioxane and 320 in the case of benzene).

Oxidation of Mesityl Oxide by Alkaline Hydrogen Peroxide.
Preparation of the Ketoxide (XI)

A solution of 150 g mesityl oxide (X) in 600 ml methanol was introduced into a three-necked flask provided with a mechanical stirrer, a thermometer and two dropping funnels; the solution was cooled with a mixture of ice and salt (-10°) and 360 ml 15% hydrogen peroxide (1 mole) and 15 ml 4 N sodium hydroxide solution were simultaneously added with continuous stirring over a period of 1.5 hours. The temperature of the solution was maintained at not higher than +5°. After a period of 20 minutes, 5 g hydrogen peroxide remained (out of 54 g), and after 50 minutes the excess of hydrogen peroxide was destroyed by addition of a little manganese dioxide. The solution was neutralized with 10% sulfuric acid, diluted with water, saturated with sodium chloride, and extracted with ether. The ether extracts were dried with magnesium sulfate, the ether was driven off, and the residue distilled in vacuum to give 68 g of hydroxy fractions (b.p. 60-65° at

21 mm), from which the ketoxide (XI) was isolated after 5 fractionations in the form of a colorless, volatile, mobile liquid with a characteristic, pleasant odor:

B.p. 62° at 22 mm; n_D^{20} 1.4223; d_4^{20} 0.9715; MR found 29.840; computed 30.06.

5.595 mg substance: 12.760 mg CO_2; 4.395 mg H_2O.
3.900 mg substance. 8.885 mg CO_2; 3.090 mg H_2O.
Found %: C 62.24, 62.17; H 8.79, 8.86.
$C_6H_{10}O_2$. Computed %: C 63.15; H 8.78.

0.1538 g substance: 16.0 g benzene: Δt 0.446°.
Found: M 113.
$C_6H_{10}O_2$. Computed: M 114.

This ketoxide formed two dinitrophenylhydrazones: one with m.p. 102-103° (from ethanol), and the other with m.p. 130-131°. The ketoxide is therefore probably a mixture of two isomers. The 2,4-dinitrophenylhydrazone with m.p. 102-103° (golden yellow platelets) is isolated in a smaller amount and probably corresponds therefore to the iso form (XIV):

4.116 mg substance: 0.678 ml N_2 (22°, 759 mm).
4.240 mg substance: 0.695 ml N_2 (21°, 758 mm).
Found %: N 19.04, 18.98.
$C_{12}H_{14}O_5N_4$. Computed %: N 19.05.

The 2,4-dinitrophenylhydrazone with m.p. 130-131° (orange crystals) is isolated in larger amount and is evidently the derivative of the ketoxide with normal structure (XI):

4.015 mg substance: 0.672 ml N_2 (23°, 748 mm).
4.295 mg substance: 0.724 ml N_2 (24°, 748 mm).
Found %: N 19.00, 19.07.
$C_{12}H_{14}O_5N_4$. Computed %: N 19.05.

The ketoxide (XI) is soluble in all of the common solvents. It is miscible with water in all ratios. It irritates the skin, causing itching and blisters.

From the high-boiling products of this experiment was isolated 5.5 g of a substance $C_6H_{12}O_3$ (an isomer of the keto glycol XII) in the form of a colorless, mobile liquid devoid of odor, with the constants:

B.p. 79-81° at 15 mm; n_D^{20} 1.4328; d_4^{20} 1.0373; MR found 33.06; computed 32.97.

6.621 mg substance: 270 mg CO_2; 5.279 mg H_2O.
3.942 mg substance: 7.860 mg CO_2; 3.166 mg H_2O.
Found %: C 54.69, 54.41; H 8.92, 8.98.
$C_6H_{12}O_3$. Computed %: C 54.54, H 9.09.

0.1419 g substance. 16.0 g benzene: Δt 0.346°.
Found: M 133.
$C_6H_{12}O_3$. Computed: M 132.

Determination of hydroxyl groups by the method of Chugaev and Tserevitinov:

0.1211 g substance: 27.0 ml CH_4 (17°, 748 mm).
0.1642 g substance: 37.8 ml CH_4 (17.5°, 748 mm).
Found %: OH 15.75, 16.28.
$C_6H_{10}C(OH)_2$. Computed %. OH 25.75.
$C_6H_9O_2(OH)$. Computed %: OH 12.88.

The 2,4-dinitrophenylhydrazone forms golden-yellow, lustrous platelets, m.p.

150-151° (from ethanol):

3.850 mg substance: 0.823 ml N_2 (20°, 756 mm).
4.110 mg substance: 0.875 ml N_2 (20°, 757 mm).
Found %: N 24.77, 24.70.
β-Dihydrazone $C_{17}H_{18}O_8N_8$. Computed %: N 24.99.

Hydration of the Ketoxide (XI). Preparation of the Keto Glycol (XII)

A solution of 15 g ketoxide (XI) in 110 ml distilled water was left overnight at room temperature. The solution was then heated for 30 minutes on a boiling water bath; after cooling, the solution was saturated with potassium carbonate and extracted with ether. The ether extracts were then dried with magnesium sulfate. After driving off the ether, the residue was distilled to give 3.5 g of hydration products from which, following two redistillations in vacuum, was isolated the keto glycol (XII) in the form of a thick, colorless, and almost odorless syrup:

B.p. 98.24° at 11 mm; n_D^{20} 1.4495; d_4^{20} 1.0809; MR found 32.789; computed 32.97.

5.335 mg substance: 10.610 mg CO_2; 4.325 mg H_2O.
6.910 mg substance: 13.745 mg CO_2; 5.485 mg H_2O.
Found %: C 54.27, 54.28; H 9.07, 8.88.
$C_6H_{12}O_3$. Computed %: C 54.54. H 9.09.

0.1657 g substance: 16.0 g dioxane: Δt 0.355°.
0.2811 g substance: 16.0 g dioxane: Δt 0.645°.
Found: M 134, 126.
$C_6H_{12}O_3$. Computed: M 132.

Determination of hydroxyl groups by the Chugaev-Tserevitinov method:

0.1199 g substance: 40.3 ml CH_4 (15.5°, 745.2 mm).
0.0391 g substance: 12.8 ml CH_4 (16°, 745 mm).
Found %: OH 23.82, 23.15.
$C_6H_{10}O(OH)_2$. Computed %: OH 25.75.

2,4-Dinitrophenylhydrazone – bright-yellow needles with m.p. 156-156.5° (from ethanol).

4.940 mg substance: 0.761 ml N_2 (23°, 759 mm).
5.190 mg substance: 0.806 ml N_2 (22°, 756 mm).
Found %: N 17.74, 17.88.
$C_{12}H_{16}O_6N_4$. Computed %: N 17.95.

Oxidation of 1-Methoxy-5-methyl-4-hexen-3-one (III) with Hydrogen Peroxide in a Medium of Anhydrous Formic Acid

332 ml perhydrol (96 g hydrogen peroxide, or 4 moles) was introduced over a period of one hour dropwise into a solution of 100 g methoxy ketone (III) in 100 ml anhydrous formic acid. The temperature of the liquid was prevented from rising above 35° by cooling with cold water. The reaction was accompanied by the evolution of carbon dioxide. The solution is left overnight at room temperature and then heated for 7 hours on a water bath at 60-70°. At the conclusion of the experiment (after 50 hours) the reaction mixture contained 18 g hydrogen peroxide.

The reaction products were separated by distillation in vacuum without neutralization. The main product of the reaction was 56 g of β-methoxypropionic acid, which has been described in the literature [9] and has the constants:

B.p. 210-212.5°; n_D^{17} 1.4237.

Yield about 70% of theory.

In addition, 5 g of acetone, b.p. 56-59°, was obtained. Not more than 2% of the theoretical amount of neutral products with constants corresponding to the ketoxide (IV) was isolated.

Oxidation of 1-Methoxy-5-methyl-4-hexen-3-one (III) by Hydrogen Peroxide in a Medium of Glacial Acetic Acid in Presence of Sulfuric Acid

Acetylhydroperoxide was prepared by dropwise addition over a period of 40 minutes at 85° of 162 g perhydrol to a mixture of 102 g glacial acetic acid and 2 g concentrated sulfuric acid. In this way a hydroperoxide is obtained with a strength of 33% and a total active oxygen content of 22.7 g.

In the course of 30 minutes 100 g methoxy ketone (III) was added to the acetyl hydroperoxide solution prepared as above. The temperature of the liquid was maintained at 22° by cooling with iced water. After standing for 36 hours at room temperature, the solution still contained 2.6 g active oxygen. After neutralization of the sulfuric acid with sodium acetate, the main bulk of the acetic acid was distilled off in vacuum. The residue was diluted with twice the volume of water when 3.8 g of crystalline neutral material was precipitated. After collection of the crystals, the filtrate was neutralized with soda and extracted with ether. The ether extracts were dried with sodium sulfate, the ether driven off, and the residue distilled in vacuum. 8 g of a liquid was obtained which corresponded to the ketoxide (IV) in properties (b.p. 78-81° at 3 mm; n_D^{27} 1.4370). The undistilled product in quantity of 20 g crystallized partially after 10 days.

After recrystallization from 50% alcohol the crystalline product melted at 105-106°.

4.350 mg substance: 8.890 mg CO_2; 3.484 mg H_2O.
4.026 mg substance: 8.216 mg CO_2; 3.150 mg H_2O.
Found %: C 55.74, 55.66, H 8.96, 8.78.
$C_{13}H_{24}O_6$. Computed %: C 56.50; H 8.70

0.1795 g substance: 12.0 g benzene: Δt 0.274°.
Found %. M 274.
$C_{13}H_{24}O_6$. Computed %. M 276.

The crystalline product did not contain free hydroxyl groups and did not form a semicarbazone. It was not saponified by alcoholic caustic alkali even on heating for 6 hours at 75°. Its structure was not established.

From the aqueous solution of salts, 21 g β-methoxypropionic acid was isolated after concentration in vacuum, acidification with concentrated hydrochloric acid, and extraction with ether.

Hydroxylation of 1-Methoxy-5-methyl-4-hexen-3-one (III) by Hydrogen Peroxide in a Medium of Anhydrous Tertiary Butyl Alcohol in Presence of Osmium Tetroxide

An anhydrous solution of hydrogen peroxide in tertiary butyl alcohol and a solution of the osmium catalyst were prepared by the method of Milas [2]. The catalyst consisted of a 1% solution of osmium tetroxide in anhydrous tertiary butanol.

To 25 g methoxy ketone (III) dissolved in an equal amount of anhydrous tertiary butyl alcohol was added 110 ml (1 mole) 5.8% anhydrous solution of hydrogen peroxide in tertiary butyl alcohol. To the solution, cooled to -3°, was added 2 ml osmium catalyst. Heat was generated during the reaction. After the evolution of heat had ceased, the flask containing the reaction mixture was removed from the cooling bath (ice + salt). After 3 hours the reaction mass contained 0.02 g hydrogen peroxide (out of 6.45 g introduced). After 40 hours the tertiary

butyl alcohol was distilled off in a low vacuum at room temperature and the residue distilled in vacuum. Two fractionations then yielded 10 g of initial methoxy ketone (III) and 2 g of thick syrup identified as the keto glycol (V); b.p. 110° at 1.5 mm; n_D^{20} 1.4555.

SUMMARY

The action of alkaline hydrogen peroxide on 1-methoxy-5-methyl-4-hexen-3-one (III) results in a yield of about 70% of ketoxide (V), hydrolysis of which leads to the keto glycol (V). The latter forms a diacetate on acetylation with acetic anhydride. The reaction of hydrogen peroxide with mesityl oxide is more complicated, yielding about 10% of ketoxide (XI) together with an isomeric ketoxide possessing in all probability the structure (XIV). Hydrolysis of the ketoxide (XI) gives the keto glycol (XII). Other methods of oxidation of aliphatic α,β-unsaturated ketones are unsuitable for the preparation of the corresponding α-ketoxides. Oxidation of the methoxy ketone (III) with the aid of hydrogen peroxide in solution of anhydrous formic acid leads to smooth splitting of the double bond and to the formation of β-methoxypropionic acid in a yield of about 75%.

Other products isolated after reaction of alkaline hydrogen peroxides with the methoxy ketone (III) and mesityl oxide, apart from the ketoxides (IV) and (IX), were 10-20% of compounds of unknown structure isomeric with the keto glycols (V and XII). In presence of alkali the ketoxide (IV) and the saturated methoxy ketone (VIII) readily condense with loss of methanol and formation of polymers. A probable mechanism for this condensation is proposed.

LITERATURE CITED

[1] N.A.Prilezhaev, Ber., 42, 4811 (1909).

[2] N.Milas, Sussman, J.Am.Chem.Soc., 58, 1302 (1936); 59, 2342 (1937).

[3] Swern, Billen, Findley, and Scanlan, J.Am.Chem.Soc., 67, 1786 (1945).

[4] Findley, Swern, and Scanlan, J.Am.Chem.Soc. 67, 412 (1945).

[5] Widmann, Ann., 400, 86 (1913).

[6] Jörlander, Ber., 50, 406 (1917).

[7] T.I.Temnikova and V.F.Martynov, J.Gen.Chem. 15, 499 (1945).

[8] Weitz and Scheffer, Ber., 54, 2327 (1921).

[9] I.N.Nazarov and V.M.Romanov, Bull. Acad. Sci. USSR, 453, 545 (1940).

[10] Harries and Pappos, Ber., 34, 2979 (1901).

[11] Stross, Monger, Finch, J.Am.Chem.Soc., 69, 1627 (1947).

[12] Nicolet and Poulter, J.Am.Chem.Soc., 52, 1186 (1930).

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THE PROBLEM OF THE ESTROGENIC ACTIVITY OF ANOL AND ITS POLYMERS. I

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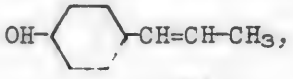
As far back as 1938 we started an investigation [1,2] of anol (p-propenylphenol) (I):



(I)

which was reported by Dodds and Lawson [3] and subsequently by Supniewsky and Hano [4] to be the simplest synthetic analog of the female sex hormone, promoting oestrus in the castrated rat when injected in quantity of 1 γ and thus approaching estrone in activity.

However, specimens of pure anol with m.p. 93°, which we prepared by demethylation of anethole with alcoholic potassium hydroxide at 200-210° proved to be 100,000 times weaker than estrone in biological tests. Also inactive was the anol benzoate which we prepared and which has likewise been reported to have estrogenic properties [3].

At the same time we found that the resinous by-products obtained during the preparation of anol possess high estrogenic activity (of the order of 100 γ). When these were fractionated in vacuum, a fraction with b.p. 200-210° at 2 mm was isolated which induced an estrogenic reaction in young mice in doses of 1 to 0.1 γ and in other physiological tests* was qualitatively and quantitatively equivalent to the natural hormone – estrone.

It was found that the brown resin obtained on heating anol at 230° for 3 hours likewise possesses estrogenic properties, and on fractionating it in vacuum a 40% fraction with activity up to 1-10 γ is obtained.

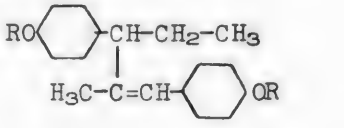
Special interest is aroused by the development of estrogenic activity on spontaneous polymerization of pure anol. The instability of anol and its ability to resinify on storage were described as far back as 1872 [5,6]. According to our own observations, the melting point of pure anol kept in a glass jar with a cork stopper falls in ten days from 93 to 63-65°, after a month it is transformed into a semi-liquid mass with an estrogenic activity of the order of 100 γ, and

*Determination of estrogenic activity was performed (Prof. K. I. Baryulin) on young female mice weighing 6-8 g. The preparation was introduced in a solution of 1 ml vegetable oil in 5 doses over a period of 60 hours; 5-6 days after the first injection, evaluation was carried out by the vaginal smear method.

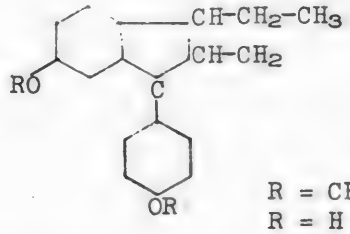
after 4 months it is completely changed into an oily liquid with an activity of 1 to 10γ .

In connection with these observations we have engaged in a study of the chemical nature of the substances which are formed during the transformation of anol and which possess estrogenic properties.

Elementary analysis and molecular weight determinations indicated that the most active fractions of the products of modification of anol – which we have called 'polyanol" – had the composition $C_{18}H_{20}O_2$, corresponding to a dimer of anol. Since not a single one of the many possible dimers of anol has been described, we prepared the following phenols (III) and (IV) from the corresponding known dimers of anethole, isoanethole or Δ^4-3,5-(p,p'-dimethoxyphenyl)-4-methylpentene [7,8] (II), and metanethole or 6,4'-dimethoxy-2-methyl-3-ethyl-1-phenylindane [9,10] (IV):



R = CH_3 (II)
R = H (III)



R = CH_3 (IV)
R = H (V)

A comparison of their properties with the properties of polyanol and its dimethyl ether revealed that the ultraviolet absorption spectra of the latter closely resembled the absorption spectra of isoanol (III) and isoanethole (II); but the specific gravities and indexes of refraction of these compounds were different, as shown by the table.

Compound	d_{25}^{25}	n_4
Isoanethole	1.0615	1.5761 (25°)
Polyanol methyl ether	1.0532	1.5570 (25°)
Isoanol	1.2840	1.5856 (45°)
Polyanol	1.2700	1.5769 (45°)

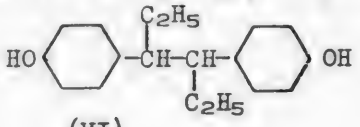
The biological tests showed that the phenol (III) is capable of inducing an estrogenic reaction in doses of not less than 100 γ, while the phenol (V) is inactive in doses of 10 mg. It was thus demonstrated that phenols corresponding to the known dimers of anethole possess a considerably lower estrogenic activity than the active fractions which we isolated.

With the aim of clarifying the structure of these active fractions we effected the oxidation of their methyl ethers with potassium permanganate under the conditions used for establishing the structure of isoanethole (II) [8]. Oxidation took place slowly and incompletely and yielded anisic acid and unsymm. p-methoxyphenylethyl acetone, which were also obtained by the oxidation of isoanethole [8]. From the unoxidized residue was separated a small amount of crystalline precipitate identified as metanethole (IV); no other crystalline materials could be isolated. Hydrogenation of polyanol using nickel catalyst yielded the dihydro compound $C_{18}H_{22}O_2$ which later on was prepared by hydrogenation of isoanethole over platinum oxide followed by demethylation of the resultant dihydroisoanethole [11].

On the basis of these observations it can therefore be suggested that the mixture of dimers of anol formed both on demethylation of anethole with potassium hydroxide and on heating anol, as well as the mixture formed during its spontaneous modification, comprises isoanol (III) and metanethole (IV) together with an unknown substance or unknown substances with the composition $C_{18}H_{20}O_2$ and

possessing high estrogenic activity.

We were unable to confirm the later statement of Campbell, Dodds, and Lawson [11,12] that the estrogenic activity of anol (I) is developed by the presence of a minute amount of meso-3,4-(p,p-dihydroxyphenyl)-hexane (VI)



(VI)

which does not affect the melting point. This compound (known also as hexoestrol and sinestrol) was isolated, they report, in the amount of 0.01% from the mixture of substances prepared by demethylation of anethole with alcoholic potassium hydroxide at 210-220°. They explained the formation under these conditions of the phenol (VI) and of small quantities of p-propylphenol as the result of hydrogenation by hydrogen which is also formed during the demethylation of anethole.

We were unable to detect the presence of phenol (VI) in our experiments on the separation of the mixture of products of demethylation of anethole (under the conditions specified by the English authors) and of the most active fractions (polyanol). The only product isolated was p-propylphenol, the formation of which under demethylation conditions may be more convincingly explained, in our opinion, by the thermal decomposition of polymers of anol in course of prolonged heating at a temperature of the order of 200°. It is known, for example, that the heating of anethole at 230° yields the methyl ethers of p-propylphenol and p-cresol [13]. It has been stated in the literature [14] that p-propylbenzene is among the products obtained on heating the polymers of p-propenylbenzene.

The suggestion of the English authors that the high estrogenic activity of anol is due to the presence of hexoestrol conflicts with our observations of the development of estrogenic properties in products of the modification of anol by spontaneous polymerization or by heating. Their explanation is also entirely inconsistent with the results of comparative studies of the biological properties of "polyanol" and sinestrol (VI) carried out by Preobrazhensky, Krasnokutskaya, and Danilova [15], as well as by Barulin, which showed, for example, that polyanol considerably surpasses sinestrol in tests on the growth of the uterus of young mice. For these reasons we are compelled to reject the theory of Campbell, Dodds and Lawson, and we consider it more probable that the estrogenic substances formed from anol are compounds of the p,p-dihydroxydiphenylpentene series.

The isolation of the individual compounds from polyanol has proved to be an extremely difficult problem. Attempts at separation through the acetates, benzoates, p-nitrobenzoates, methyl ethers and urethanes, as well as by chromatography, did not lead to the preparation of crystalline compounds. Only after a benzene solution of polyanol had been allowed to stand for six months was a crystalline material separated which melted after repeated recrystallization at 97-99°. The same substance was isolated by working up with benzene the fraction of polyanol with b.p. 199-200° at 1 mm. The benzoates of these products melted at 126.5-127°, and the m.p. of their mixture was not depressed. Nor was there any depression of the m.p. of their mixed p-nitrobenzoates (164°) and methyl eters (39-41°). Oxidation of the methyl ethers of these substances with potassium permanganate gave anisic acid and α-(p-methoxyphenyl)-propylmethyl ketone, which were obtained, as already noted, by the oxidation of isoanethole (II). Hence, the crystalline methyl ether also has the structure of Δ^4-3,5-(p,p-dihydroxyphenyl)-4-methylpentene, and the crystalline substance isolated from polyanol has the structure of Δ^4-3,5-(p,p-dihydroxyphenyl)-4-methylpentene. Still unexplained is the relation between the crystalline compounds which we have prepared and the already known liquid isoanethole (II) and the corresponding

phenol (III). The latter would appear not to be individual substances, but a mixture of isomers.

Indirect confirmation of these views is provided by the fact that the dimerization of anol or anethole by an alcoholic solution of HCl may yield, depending upon the dimerization conditions, either liquid or crystalline dimers which form identical oxidation products. Thus, on conducting the preparation of isoanethole under conditions less drastic that those applied by Goodall and Haworth [8], we obtained crystalline isoanethole with m.p. 39-41° instead of liquid isoanethole (II); by careful reaction of alcoholic HCl with pure, freshly prepared anol we obtained a good yield of crystalline Δ^4-3,5-(p,p-dihydroxyphenyl)-4-methylpentene with m.p. 99-101°.

An investigation of the substances formed by demethylation of anethole with potassium hydroxide is in progress.

EXPERIMENTAL

Dimethylation of anethole. 750 g anethole, 1100 g potassium hydroxide, and 2100 ml ethyl alcohol were heated in a 5-liter autoclave with a stirrer at 200-205° for 40 hours. During the first day of heating the pressure in the autoclave rose to 37-40 atmospheres. On the following morning the excess pressure was released from the cooled autoclave and the heating continued with intermissions at night and release of the gaseous reaction products. The solid reaction mass was dissolved in 2 liters of water and the alcohol and the unreacted anethole (100-120 g) distilled off in steam. The aqueous alkaline solution was filtered off and carefully neutralized with 25% sulfuric acid to a weak reaction with congo red. The resultant thick, oily layer was separated, dissolved in ethylene dichloride, washed with water, and dried with sodium sulfate. The solvent was removed by distillation and the residue distilled in vacuum at 1-2 mm to give three fractions.

The first fraction with b.p. 109-115° (186 g) crystallized almost entirely in the receiver. Anol with m.p. 93° was obtained from it by recrystallization from chloroform.

The second fraction (polyanol) with b.p. 210-225° (256 g) is a thick, light yellow oil, easily soluble in ether, benzene, ethylene dichloride, etc. It induces an estrogenic reaction in young female mice and rats in doses of 1-0.1 γ.

d_{25}^{25} 1.1270; n_D^{50} 1.5738.

2.815 mg substance: 8.297 mg CO_2; 1.8615 mg H_2O.
Found %: C 80.38; H 7.40.
$C_{18}H_{20}O_2$. Computed %: C 80.55; H 7.51.

Molecular weight, (Rast), 271; $C_{18}H_{20}O_2$ computed, 268.16.

The third fraction with b.p. 245-246° (96 g) is a brownish-red solid resin, completely soluble in chloroform and possessing an estrogenic activity of the order of 100 γ.

Spontaneous polymerization of anol. Anol with m.p. 93° which had been recrystallized from chloroform was kept in a glass jar with a cork stopper at room temperature for 10 days. The melting point had then fallen to 63-65°. After a month it had changed into a semi-liquid mass, and after 4 months the contents of the jar consisted of a fairly mobile reddish-brown liquid not completely soluble in chloroform and possessing an estrogenic activity of 1-10 γ.

We collected the following fractions on distillation in a 1 mm vacuum of 50 g of the products of modification of the anol fraction [1] obtained in the above manner. first fraction: up to 125°, 15 g; second fraction: 125-132°, 16.4 g

crystallized; third fraction: 220-240°, 8.7 g, n_D^{45} 1.5557 (anol).

Intensive decomposition commenced with further heating with violent evolution of gaseous products.

The fraction with b.p. 220-240° is active in a dose of 1-0.1 γ.

Thermal polymerization of anol. 90 g pure anol (m.p. 93°) was heated on an oil bath for 3 hours at 230°. The resultant transparent orange resin had an estrogenic activity of about 100 γ. Fractionation in a 3 mm vacuum gave: first fraction, 70-140°, 35.6 g (anol); second fraction, 232-240°, 34 g, n_D^{50} 1.5640; third fraction 240-262°, 16.5 g.

The fraction with b.p. 232-240° was active in doses of up to 0.1 γ.

On heating anol in a sealed tube at 210° for 10 hours a solid orange-red resin was obtained which possessed an activity of the order of 100 γ.

Methyl ether of polyanol. 20 g polyanol (second fraction) was dissolved in 30 ml of 20% sodium hydroxide solution by heating at 45°, and to the cooled solution was added 30 g dimethyl sulfate in small portions with stirring; the reaction mixture was kept alkaline by addition of sodium hydroxide solution. The mixture was then heated for 30 minutes at 60°. The separated oily layer was extracted with ether, washed with 5% sodium hydroxide solution and then with water and dried with sodium sulfate. The ether was driven off and the residue distilled in vacuum to give 16 g of a fraction with b.p. 189-192° at 1 mm and forming a thick, oily liquid:

d_{25}^{25} 1.0532; n_D^{25} 1.5570.

2.618 mg substance: 7.791 mg CO_2; 1.922 mg H_2O.
Found %: C 81.16; H 8.21.
$C_{20}H_{24}O_2$. Computed %: C 81.2; H 8.17.
Molecular weight (Rast) 303; computed 296.2.

Isoanol. Δ^4-3,5-(p,p-hydroxyphenyl)-4-methylpentene (III)

a) From isoanethole. 100 g isoanethole prepared by the method of Goodall and Haworth [8] was heated in a stirring autoclave with 150 g potassium hydroxide and 300 ml alcohol at 210-215° for 18 hours. After solution of the reaction mass in water, distillation of the alcohol and extraction with ether of the unreacted isoanethole, the alkaline solution was acidified with 20% sulfuric acid; the separated oil was extracted with ether; the extract was washed with water and dried with sodium sulfate. The solvent was then distilled off and the residue distilled in vacuum. A fraction with b.p. 210-212° at 1 mm (57 g) was collected in the form of a thick, light-yellow, noncrystallizing oil; n_D^{25} 1.5856; d_{25}^{25} 1.280; it was active in doses of 100 γ.

b) From polyanol. On keeping a solution of 100 g polyanol in 100 ml benzene in a refrigerator (+2°) for a long period, a crystalline precipitate was formed; it was filtered off on a Buchner funnel through a layer of cloth and washed with benzene. 51 g of a brownish-grey crystalline powder was obtained; after 4 crystallizations from benzene it was obtained as slightly greyish needles with m.p. 97-99°.

c) On repeated fractionation of polyanol in vacuum a fraction boiling at 190-200° at 1 mm was obtained in the form of a pale-yellow oil which crystallized when benzene was added. After recrystallization from benzene, crystals with m.p. 99-101° were obtained; a mixed specimen did not depress the melting point of the substance prepared as above.

d) From anol. A solution of 25 g pure anol in 33 ml alcohol was heated on a water bath with 70 ml 12% alcoholic HCl at 50° for 30 minutes; the mixture was diluted with 750 ml water, the separated oil was extracted with ether, and the

ether solution washed with water until the acid reaction to congo red had disappeared. After drying with sodium sulfate and driving off the solvent, the residue solidified on standing, and even more rapidly on addition of a few drops of benzene, to a crystalline mass with m.p. after recrystallization from benzene of 99-101°.

3.057 mg substance: 9.021 mg CO_2; 2.036 mg H_2O.
2.187 mg substance: 9.419 mg CO_2; 2.140 mg H_2O.
Found %: C 80.43, 80.60; H 7.45, 7.51.
$C_{18}H_{20}O_2$. Computed %: C 80.50; H 7.50.

Methyl ester of isoanol or Δ^4-3,5-(p,p-dimethoxyphenyl)-4-methylpentene (II). Crystalline isoanol was treated with dimethyl sulfate in presence of caustic alkali. After the reaction product had been worked up in vacuum in the usual manner, a fraction was isolated with b.p. 165-167° at 2 mm in the form of a pale-yellow, viscous oil which crystallized on standing. After two recrystallizations from methyl alcohol, it formed a white, finely crystalline powder with m.p. 39-41°.

The same compound was obtained by heating 125 g anethole for 10 hours in 500 ml of a 12% solution of HCl in methyl alcohol. The mixture was then run into 2 liters of water and the separated oil was distilled in vacuum. The fraction (84 g) with b.p. 163-164° at 1 mm solidified to a crystalline mass from which, after recrystallization, was obtained 61 g of a compound with m.p. 39-41°.

3.456 mg substance: 10.316 mg CO_2; 2.410 mg H_2O.
4.537 mg substance: 13.561 mg CO_2; 3.190 mg H_2O.
Found %: C 81.41, 81.5; H 7.80, 7.80.
$C_{20}H_{24}O_2$. Computed %: C 81.02; H 8.17.

Isoanol acetate. 1 g isoanol was acetylated with acetic anhydride by the Chattaway method [16]. Distillation in vacuum gave a fraction with b.p. 214-215° at 1 mm in the form of a slightly yellowish viscous oil.

4.539 mg substance: 12.531 mg CO_2; 2.920 mg H_2O.
Found %: C 75.29; H 7.20.
$C_{22}H_{24}O_4$. Computed %: C 74.96; H 6.87.

Isoanethole p-nitrobenzoate. A solution of crystalline isoanol in pyridine was treated with the theoretical amount of a benzene solution of p-nitrobenzoyl chloride. Light-yellow crystals with m.p. 164° (from butyl alcohol).

5.925 mg substance: 0.264 ml N_2 (19°, 733 mm).
6.535 mg substance: 0.294 ml N_2 (19°, 733 mm).
Found %: N 5.02, 5.07.
$C_{32}H_{26}O_8N_2$. Computed %: N 4.94.

Isoanol benzoate was prepared from crystalline isoanol and benzoyl chloride in pyridine solution. M.p. 127°.

Metanethole. (6,4'-dimethoxy-2-methyl-3-ethyl-1-phenylindane) (IV). Preparation was effected by a slightly modified Perrenoud method [9]. Anethole was heated in an iron pot (with a stirrer) with 2.5 parts zinc chloride and 5 parts petroleum jelly at 150-155° for 8 hours. The reaction mass was treated with water, the separated oil was washed with hot water, dried, and fractionated in vacuum. A fraction with b.p. 180-220° at 3 mm was collected and partially crystallized. It was treated with alcohol and recrystallized from glacial acetic acid to give anethole in the form of soft needles, m.p. 132-133°.

Demethylation of metanethole – preparation of 6,4'-dihydroxy-2-methyl-3-ethyl-1-phenylindane (V). To a solution of ethyl magnesium iodide, prepared from 2.43 g magnesium, 5.6 g methyl iodide and 40 ml ether, was added a solution of 10 g metanethole in 80 ml isoamyl ether. After driving off the ethyl ether,

the mixture was heated for 8 hours at 180°. The cooled mixture was worked up with 5% sulfuric acid and then washed with water. The isoamyl ether was distilled off at 15 mm and the residue distilled at 1 mm. A fraction with b.p. 190-200° was collected in the form of a light-yellow waxy mass, recrystallization of which from gasolene (b.p. 80-100°) yielded a slightly greyish crystalline powder with m.p. 156°.

3.864 mg substance: 10.111 mg CO_2; 2.20 mg H_2O.
Found %: C 80.40; H 7.35.
$C_{18}H_{20}O_2$. Computed %: C 80.55; H 7.51.

Examination of metanethole by the Allen-Doisy test showed it to be inactive in doses of up to 10 mg.

Oxidation of polyanol methyl ether. Into a three-necked flask provided with a thermometer and mechanical stirrer was introduced a solution of 50 g methyl ether of polyanol (n^{25} 1.5568) in 1 liter acetone and 48 g sodium bicarbonate, and while stirring energetically 48 g pulverized potassium permanganate was added in small portions. The temperature of the reaction mixture was maintained at 10-14°. When all had been added, the mixture was further stirred for 4 hours, after which the precipitated manganese dioxide and salts were filtered off and the solvent distilled off (towards the end in vacuum). The residual oil (34 g) was dissolved in 70 ml alcohol and to this solution was added a solution of 6 g semicarbazide hydrochloride and 6 g sodium acetate in 20 ml alcohol. The mixture was heated on the water bath for 3 hours and then diluted with water. The resultant crystalline precipitate of semicarbazone was filtered off, washed with ether and recrystallized from methyl alcohol to give 4.3 g of a semicarbazone with m.p. 188-189° and not depressing the m.p. of the semicarbazone of α-(p-methoxyphenyl)-p-propylmethyl ketone obtained by oxidation of isoanethole under similar conditions.

Unoxidized polyanol methyl ether (29.2 g) was recovered from the aqueous alcoholic filtrate by extraction with ether. After distillation in vacuum it had the same physical properties as the original material.

The precipitate of manganese dioxide was washed with hot water, the wash liquors were concentrated to a small volume and acidified with hydrochloric acid. The resultant precipitate was filtered off and recrystallized from water to give 4.3 anisic acid with m.p. 184°.

Repetition of the above process with the unreacted polyanol methyl ether under the same conditions yielded a further quantity of α-(p-methoxyphenyl)-p-propylmethyl ketone and anisic acid. The unoxidized residue after a third oxidation (9.4 g) had d_{25}^{25} 1.0588 and n_D^{25} 1.5567. After standing for a long period at 0° it deposited crystals (0.3 g) which after recrystallization from acetic acid melted at 131° and did not depress the m.p. of metanethole. Subsequently the filtrate from the metanethole deposited a very small amount of acicular crystals which melted at 215-217.5° (from alcohol).

Hydrogenation of polyanol. 10 g polyanol in 150 ml alcohol was hydrogenated in a stirring autoclave in presence of 3 g Raney catalyst and at a pressure of 60 atmospheres and a temperature of 120°. After removing the catalyst and distilling off the solvent, the residue was dissolved in ether and the ethereal solution worked up with 10% sodium hydroxide solution. The substance precipitated on acidification of the alkaline solution was extracted with ether, the ether was driven off and the residue distilled in vacuum. There was obtained 6.3 g of solid vitreous mass (b.p. 216-225° at 2 mm) which crystallized on standing. Recrystallization from alcohol yielded dihydrodianol with m.p. 128°. This is the same as the m.p. of the dihydrodianol prepared by Campbell, Dodds, and Lawson [11] by hydrogenation of isoanethole and subsequent demethylation.

SUMMARY

1. The demethylation of anethole with potassium hydroxide was investigated.

2. Among the products of demethylation was a fraction possessing estrogenic activity approaching that of the natural hormone, estrone; the optimum conditions for its preparation were established.

3. It was found to consist of a mixture of dimers of anol.

4. A previously undescribed crystalline dimer of anol was isolated: Δ^4-(3,5-p,p-dimethoxyphenyl)-4-methylpentene.

5. It was shown that substances with estrogenic activity are also formed by spontaneous polymerization of anol and by the action of heat.

LITERATURE CITED

[1] K.I.Barulin, Kerov, and others, Problems of Fecundity of Horses. (Collection NKZema, 1939, p. 76).

[2] K.I.Barulin and Kerov, Horse-breeding, 1941, p. 18.

[3] E.C.Dodds, W.Lawson, Nature, 139, 627 (1937).

[4] J.W.Supniewsky and J.Hano. Bull. Intern. acad. polon. sci., Classe med., 1937, 487; Chem. Abs., 33, 8294 (1939).

[5] A.Ladenburg, Spl. VIII, 88 (1872).

[6] R.Stoermer and B.Kahlert, Ber., 34, 1812 (1901).

[7] Kraut, Schlun. Jahresbericht uber die Fortschritte der Chemie. 552 (1863).

[8] G.D.Goodall and R.D.Haworth, J.Chem.Soc., 2482 (1930).

[9] P.Perrenoud, Ann., 187, 68 (1877).

[10] W.Baker and J.Enderby, J.Chem.Soc., 1940, 1091.

[11] N.R.Campbell, E.C.Dodds, W.Lawson, Proc. Roy.Soc. (London), 128, 253 (1939-1940).

[12] E.C.Dodds, J.Goldbery, E.J.Grünfeld, W.Lawson, C.M.Saffer, and R.Robinson, Proc. Roy. Soc. (London), 132, B 83-101 (1944).

[13] Orndorff, Terrasse, Morton, J.Am.Chem.Soc. 19, 862 (1891).

[14] Dreyer, Ann., 517, 77 (1935).

[15] A.P.Preobrazhensky, M.P.Danilova, and O.V.Krasnokutskaya, Pharmacology and Toxicology, VII, No. 2, p. 49 (1944).

[16] Chattaway, J.Chem.Soc., 1931, 2495.

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THE CONDENSATION OF Py-INDOLEALDEHYDES WITH MALONIC ACID AND ETHYL CYANOACETATE

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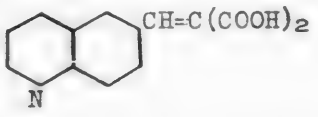
In 1926 Rodionov and coworkers [1] discovered a very simple method of preparation of β-aryl-β-amino acids, consisting of the reaction of aromatic aldehydes with malonic acid in presence of alcoholic ammonia:

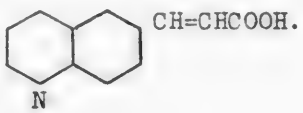
$$RCHO + NH_3 + CH_2(COOH)_2 \longrightarrow RCH(NH_2)-CH_2COOH + H_2O + CO_2.$$

This method was subsequently extended to aliphatic aldehydes [2], and it was shown that the method was generally applicable both to the aromatic and aliphatic series.

The reaction has not been systematically investigated in relation to aldehydes of the heterocyclic series. Isolated experiments have been made with 2-furaldehyde and with all of the Bz-aldehydes of the quinoline series. Condensation does not take place with 2-furaldehyde and considerable resinification occurs. Condensation with quinolinic aldehydes does not take place smoothly, and the main reaction products are quinolylacrylic and quinolylethylene dicarboxylic acids, for example:



and



The yields of β-quinolyl-β-aminopropionic acids were low.

In the present investigation the study of condensation with malonic acid has been extended to the following four most readily accessible indolealdehydes: indole-3-aldehyde; 1-methylindole-3-aldehyde; 2-methylindole-3-aldehyde; and 1,2-dimethylindole-3-aldehyde.

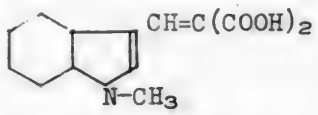
The first three aldehydes were prepared by the literature methods. The preparation of 1,2-dimethylindole-3-aldehyde by reacting methylformylaniline with 1,2-dimethylindole [3] is rather involved. This aldehyde was synthesized more simply by the methylation of 2-methylindole-3-aldehyde with excess of dimethyl sulfate in an alkaline medium with a yield of up to 80% of theory.

The indolealdehydes vary in their behavior during condensation with malonic acid under the usual conditions: indole-3-aldehyde and 2-methylindole-3-aldehyde

do not enter into reaction; in the condensation with 2-methylindole-3- aldehyde the reaction mass becomes a bright cherry red.

1-Methylindole-3-aldehyde gives a 77-78% yield of a yellow compound with m.p. 182-183°.

Recrystallization from alcohols gave green platelets with the same melting point. The structure of the compound was elucidated, and it proved to be 1-methylskatolidene malonic acid, not previously described in the literature:



When heated with dimethylaniline this compound is fairly readily decarboxylated with formation of β-(1-methylindolyl-3)-acrylic acid with m.p. 163-164°. Methylindolyl acrylic acid has likewise not been described in the literature. A by-product obtained in small amount is a substance with m.p. 73-74° which is very unstable when stored and is apparently methylindolylethylene.

1,2-Dimethylindole-3-aldehyde is recovered almost in its entirety from the reaction product. The reaction mass became cherry-colored.

Examination of the reaction product revealed the presence in negligible amount of two acids: one with a yellow color, m.p. 154-156°, was insoluble in hot benzene, and had an acid value of 135; the second was white, soluble in hot benzene, and had an acid equivalent of 208; m.p. 156-159°.

A preliminary examination suggests that the first acid is dimethylskatolidene malonic acid (acid value 129.6), while the second may be dimethylindolylacrylic acid (acid value 215.0).

Thus, under the conditions of reaction used by Rodionov neither of the above indolealdehydes gave the corresponding β-amino acids, and only in one case (with 1-methylindole-3-aldehyde) was the corresponding unsaturated dicarboxylic acid isolated in good yield.

An attempt was subsequently made to prepare β-amino-β-(1-methylindolyl-3)-ethane-α,α-dicarboxylic acid under the conditions proposed by Mannich and Ganz [4] for the synthesis of β-aminodicarboxylic acids, i.e., by prolonged standing at room temperature. Experiments showed that under these conditions 1-methylindole does not enter into reaction; hence we may assert that even if a β-aminodicarboxylic acid is formed on heating, its instability will cause it to lose ammonia with conversion into 1-methylskatolidene malonic acid.

The study of the reaction of indolealdehydes with malonic acid revealed the marked influence of the presence and position of methyl groups upon the reactivity of the aldehydes. Those in which the nitrogen is methylated react more readily, the presence of a methyl group at the second carbon atom hinders condensation.

The validity of these observations was checked by carrying out condensations of the same aldehydes with malonic acid by Döbner's procedure (i.e., in a pyridine medium with piperidine as catalyst), and also with cyanoacetic ester as a compound possessing a highly reactive methylene group.

The Döbner condensation was performed under conditions similar to those recommended for indole-3-aldehyde [5]: the mixture of aldehyde, malonic acid, pyridine, and piperidine was heated for about 40 hours at 38-40°. It is interesting to note that the reaction mass turned a cherry color when 2-methylindole-3-aldehyde and 1,2-dimethylindole-3-aldehyde were used. Confirmation was thus obtained of the observation that aldehydes not possessing a methyl group at the second carbon atom have a greater reactivity. Thus, indole-3-aldehyde gives a 31.6%

yield of β-indolylacrylic acid; 1-methylindole-3-aldehyde gives a mixture of 1-methylskatolidene malonic acid and 1-methylindolyl acrylic acid in a total yield of 50% of theory, while 2-methylindole-3-aldehyde and its N-methyl derivative give negligible amounts of substances of acidic character, the structure of which could not be established owing to lack of starting material.

Condensation with ethyl cyanoacetate was carried out at room temperature: an alcoholic solution of the aldehyde, ethyl cyanoacetate and piperidine was allowed to stand for 48 hours. All of the four aldehydes yielded normal products of reaction - the ethyl esters of the corresponding α-cyano-β-(indolyl-3)-acrylic acids.

In the case of indole-3-aldehyde and its N-methyl derivative, the condensation products separate in large quantity after only an hour and the yields approach the quantitative figures.

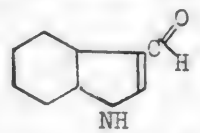
Under the same conditions the reaction with the 2-methyl aldehyde commences only after 3 hours and the yield of the acrylic acid derivative does not exceed 26-27% of the theoretical. With 1,2-dimethylindole-3-aldehyde the separation of precipitate commences after 30 hours and the yield is 37-38% of theory.

The experimental results are summarized in the table.

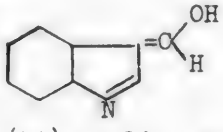
No.	Aldehyde	Yield of condensation products		
		With malonic acid (allowing for unreacted aldehyde		With ethyl cyanoacetate (calculated on initial aldehyde
		Rodionov's method	Döbner's method	
1	Indole-3-aldehyde	0.0	31.6	91.9
2	1-Methylindole-3-aldehyde....	77.6	50.0	93.7
3	2-Methylindole-3-aldehyde....	0.0	Traces	26.3
4	1,2-Dimethylindole-3-aldehyde	2.3	Traces	37.7

The superior condensing ability of the N-methylated indolealdehydes is in agreement with the observations of Majima and Kotake [6] who carried out the reaction of indole-3-aldehyde with nitromethane in an alkaline medium and only obtained a condensation product after previous acetylation of the aldehyde at the nitrogen atom.

This change in the activity of the aldehyde can probably be explained by the ability of this compound to exist in two tautomeric forms:



(I) aldehydic, indole form



(II) enolic, pseudo-indole-form

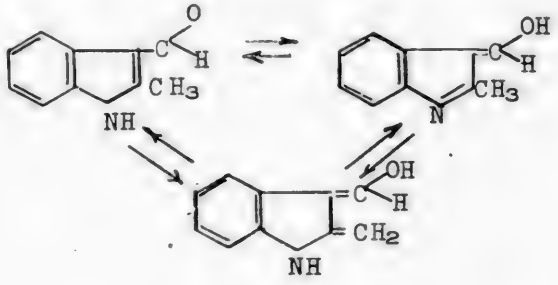
The conditions of our experiments - presence of an alkaline medium - promote enolization of the aldehyde, i.e., formation of the pseudoindole (II). The presence of a methyl group at the nitrogen atom excludes the possibility of formation of the pseudoindole form, the compound reacts in its aldehydic form, and condensation reactions proceed more readily and with better yields.

On this hypothesis many of the reactions of indolealdehyde become understandable. It explains, for example, why it does not give the reactions of Cannizzaro [6] and Perkin or the benzoin condensation [7]. Evidence also exists of the reduced reactivity of 2-methylindole-3-aldehyde. Thus it does not react with hydantoin [8], whereas indole-3-aldehyde and its N-methyl derivative give the respective condensation products in good yield [9]. 2-Methylindole-3-aldehyde reacts with benzyl cyanide with great difficulty, only when heated in a

sealed tube [10], while N-methylindol[illegible]-3-aldehyde and indole-3-aldehyde condense easily with formation in good yield of the nitriles of the corresponding α-phenyl-β-indolylacrylic acids [7].

The most probable explanation of the reduced condensing ability of 2-methylindole-3-aldehyde is, primarily, that it is the result of the usual type of tautomerism of compounds with a methyl or methylene group in the α- and γ-positions to the carbonyl group, and secondly that it is the result of the indole-pseudoindole tautomerism which is characteristic of the aldehydes of this series with a CHO group at the third carbon atom.

The above theory is also supported by the development of a deep color which is characteristic of compounds containing a similar system of conjugated double bonds, and which was noted in unsuccessful attempts to condense 2-methylindole--3-aldehyde and its N-methyl derivative in an alkaline medium.



In respect of indole-3-aldehyde and 1-methylindole-3-aldehyde, such a coloration was never observed in a single instance, and condensation products were obtained.

It is interesting to note that no color is developed in the reaction of 2-methylindole-3-aldehyde and its N-methyl derivative with ethyl cyanoacetate, and products of condensation involving the aldehyde group were obtained in satisfactory yields.

EXPERIMENTAL

I. Synthesis of the Initial Aldehydes

1. Indole-3-aldehyde was prepared by the method of Boyd and Robson: the action of potassium hydroxide on an alcohol solution of indole and chloroform when heated [11]. M.p. 190-192°; yield 30% of theory.

2. 1-Methylindole-3-aldehyde was synthesized by Wieland's method [13]: methylation of indole-3-aldehyde with dimethyl sulfate in an alkaline medium. We increased the yield of methylation product from 68% to 95.3%.

At a temperature of 50-60° and with intensive shaking, gradual addition was made over a period of an hour of [illegible] g freshly distilled dimethyl sulfate to a mixture of 25.1 g indole-3-aldehyde and [illegible].7 g sodium hydroxide in 750 ml water. After the addition was completed, shaking was continued for another 4 hours. On the following day the yellow precipitate of methylated product was filtered off, washed with water until neutral to litmus, and then with ether. There was obtained 23.6 g of aldehyde with m.p. 69-70° (Wieland gives 65°).

A further 2.6 g material was recovered from the ether washings, making a total of 26.2 g, or 95.3% of theory.

3. 2-Methylindole-3-aldehyde was prepared by the method of Boyd and Robson [11], consisting in reaction of excess chloroform and potassium hydroxide with 2-methylindole in an aqueous alcoholic medium.

a) 2-Methylindole (methylketol) was prepared, in accordance with the patented method, by cyclization of acetone phenylhydrazone (as described by Fischer) in presence of anhydrous $ZnCl_2$, using cumene as solvent [12]. Yield 71.5% of theory.

b) 2-Methylindole-3-aldehyde was prepared in 49.7% yield (Boyd and Robson claim 50%); m.p. 198-200°.

4. 1,2-Dimethylindole-3-aldehyde was prepared by methylation of 2-methylindole-3-aldehyde with dimethyl sulfate in an alkaline medium. To a heated solution (60°) of 51 g potassium hydroxide in 1 liter water was added 10 g aldehyde, and then 96 g freshly distilled dimethyl sulfate was introduced with intensive shaking over a period of 3 hours. After about one-fifth of the dimethyl sulfate had been added, rapid clouding of the solution was observed, accompanied by separation of a flocculent precipitate. The next day the yellow precipitate of the N-methyl derivative was filtered off, washed with water and ether. 0.5 g of the original aldehyde was recovered from the ether washings. There was obtained 10.5 g of methylated product with m.p. 115-125°. One recrystallization from alcohol yielded 8.3 g with m.p. 128-130°, corresponding to 76.1% of the theoretical, or 80% allowing for the aldehyde which had not reacted.

After repeated recrystallization the melting point of the product did not rise above 131° (the literature gives m.p. 132°).

Analysis of compound with m.p. 131°:

4.16 mg substance: 11.67 mg CO_2; 2.43 mg H_2O.
Found %: C 76.49; H 6.53.
$C_{11}H_{11}ON$. Computed %: C 76.27; H 6.40.

3.93 mg substance: 0.287 ml N_2 (26°, 745 mm).
3.26 mg substance: 0.241 ml N_2 (26°, 746 mm).
Found %: N 8.17; 8.28.
$C_{11}H_{11}ON$. Computed %: N 8.09.

II. Condensation of Indolealdehydes with Malonic Acid in a Medium of Alcoholic Solution of Ammonia

1. Indole-3-aldehyde. Two experiments with different heating periods were performed. Using identical ratios of starting materials – aldehyde, malonic acid, and ammonia – heating was effected for 5 hours in one case and for 17 hours in the other.

The results of the two experiments were identical: 1) The main bulk of aldehyde was recovered unchanged, although considerable resinification took place in the 17-hour experiment; 2) traces of an acidic substance were isolated but identification was impossible owing to the small amount.

We give details of the first experiment only:

A mixture of 2 g aldehyde, 1.6 g malonic acid, and 5 ml 7% alcoholic solution of ammonia was heated on a water bath, using a reflux condenser. At the end of two hours the whole of the aldehyde was dissolved, and at the end of the fifth hour a dark, viscous mass had formed. It was worked up on the following day with 10% sodium carbonate solution.

Residue insoluble in sodium carbonate. Weight 1.7 g, m.p. 163-180°. After repeated washing with ether and one recrystallization from alcohol it did not depress the m.p. of the original aldehyde.

The soda filtrate was freed from resinous admixtures by ether extraction, and was then acidified with dilute hydrochloric acid. The transparent hydrochloric acid solution was evaporated to dryness. The dry residue was examined for its amino acid content. After prolonged standing in a desiccator over concentrated sulfuric acid, it was worked up with absolute alcohol. To the alcoholic extract was added absolute ether. On standing for many days a small quantity of precipitate with m.p. 130-131° was obtained which did not depress the melting point of malonic acid.

2. 1-Methylindole-3-aldehyde. Several experiments were carried out with

variations in the ratios of starting materials and the duration of heating. In all instances the sole reaction product was an acidic substance melting at 182-183°.

A mixture of 8 g aldehyde, 5.8 g malonic acid and 18 ml 7% ammonia solution was heated for 3 hours on a water bath under a reflux condenser. An hour after the commencement of heating the contents of the flask suddenly crystallized. On the following day the solid was filtered off from the alcoholic solution.

a) Treatment of solid. It was washed with a little alcohol and treated with 10% soda solution. The soda solution was extracted with ether and acidified with dilute hydrochloric acid. The resultant bright-yellow precipitate formed green platelets after recrystallization from alcohol; m.p. with decomposition 182-183°. Weight of precipitate 3.65 g.

The alcoholic filtrate after recrystallization of the solid was evaporated down and the residue treated with soda solution to give 0.6 g of the original aldehyde. The soda filtrate yielded a further 0.1 g substance with m.p. 182-183°.

The solid product thus yielded, in all, 3.75 g green substance with m.p. 182-183°, and 0.6 g original aldehyde.

The hydrochloric acid filtrate obtained after removal of the yellow solid was examined as in the preceding experiment for its content of amino acid.

In order to obtain more precise results, the filtrates from several experiments were examined. Just as in the case of indole-3-aldehyde, the dry residue yielded only a small amount of malonic acid.

b) Working up of the alcoholic filtrate. The main bulk of alcohol was distilled off, and the residue treated with soda. The soda-insoluble residue weighed 3.4 g after washing with ether and did not depress the melting point of the original aldehyde. After several reprecipitations and recrystallizations from alcohol, the soda filtrate yielded 0.4 g green material with m.p. 181-182°.

In all, the condensation of 1-methylindole-3-aldehyde with malonic acid by the Rodionov procedure gave 4.15 g substance with a green color and m.p. 182-183° while 0.4 g unreacted aldehyde was recovered. The yield of product, calculated on the 1-methylskatolidene malonic acid, was 77.6%, allowing for the unreacted aldehyde.

Analysis of substance with green color and m.p. 182-183°:

3.91 mg substance: 9.11 mg CO_2; 1.60 mg H_2O.
3.71 mg substance: 8.67 mg CO_2; 1.55 mg H_2O.
Found %: C 63.54, 63.73; H 4.58, 4.67.
$C_{13}H_{11}O_4N$. Computed %: C 63.67; H 4.49.

3.68 mg substance: 0.184 ml N_2 (25°, 745 mm).
4.65 mg substance: 0.230 ml N_2 (25°, 745 mm).
Found %: N 5.61, 5.56.
$C_{13}H_{11}O_4N$. Computed %: N 5.71.

0.1808 g substance: consumed 14.5 ml 0.1 N NaOH.
0.2556 g substance: consumed 20.7 ml 0.1 N NaOH.
1.1898 g substance: consumed 15.3 ml 0.1 N NaOH.
Equivalent, found: 124.7, 123.4, 123.9.
Equivalent calculated for 1-methylskatolidene malonic acid: 122.57.

Analysis of Ag salt: 0.2538 g substance: 0.1184 g Ag.
0.2980 g substance: 0.1397 g Ag.
Found %: Ag 46.65; 46.84.
$C_{13}H_9O_4NAg_2$. Computed %: Ag 47.05.

Heating of 1-Methylskatolidene Malonic Acid in Dimethylaniline

Experiment 1. A mixture of 75 ml of freshly distilled dimethylaniline and 5 g 1-methylskatolidene malonic acid was heated under a reflux condenser on a glycerol bath. Vigorous evolution of carbon dioxide commenced at a bath temperature of 80° and was completed after 10-15 minutes. The mass was then heated for a further 45 minutes, the temperature of the bath being slowly raised to 160°. After cooling, the mass was worked up with 15% soda solution.

The dimethylaniline layer was separated from the soda layer and treated with dilute hydrochloric acid. The dimethylaniline went into solution and a minute amount of highly resinous solid with m.p. 65-70° was separated. (See experiment 2 for purification and attempted identification).

The separated hydrochloric acid filtrate was rendered alkaline, the separated layer was removed and distilled in steam. There was obtained 60 ml dimethylaniline and about 0.5 g resin in the flask. The residue was not further investigated.

The soda extract was extracted with ether and acidified with dilute hydrochloric acid. Even when the reaction to litmus was still slightly alkaline, a white substance with m.p. 159-161° began to separate. Weight 1.3 g. No further separation of the yellow precipitate of the original acid was observed with further acidification until acid to litmus.

The white substance melted at 163-164° after recrystallization from 50% alcohol.

4.48 mg substance: 11.72 mg CO_2; 2.02 mg H_2O.
Found %: C 71.35; H 5.05.
$C_{12}H_{11}O_2N$. Computed %: C 71.67; H 5.51.

5.465 mg substance: 0.322 ml N_2 (25°, 747 mm).
4.287 mg substance: 0.257 ml N_2 (21°, 746 mm).
Found %: N 6.63, 6.86.
$C_{12}H_{17}O_2N$. Computed %: N 6.97.

0.0536 g substance: consumed 2.62 ml 0.1 N NaOH.
0.1480 g substance: consumed 7.38 ml 0.1 N NaOH.
Equivalent, found: 204.5, 200.0.
Equivalent calculated for methylindolylacrylic acid ($C_{12}H_{11}O_2N$): 201.2.

Analysis for Ag salt: 0.1600 g substance: 0.0562 g Ag.
Found %: Ag 35.12.
$C_{12}H_{10}O_2NAg$. Computed %: Ag 35.02.

Experiment 2. A mixture of 30 ml dimethylaniline and 3 g methylskatolidene malonic acid was heated on a glycerol bath at 120-130°. After 25-30 minutes, as soon as the vigorous evolution of carbon dioxide had ceased, the heating was concluded, and the reaction mass worked up as in Experiment 1.

Acidification of the soda layer yielded a negligible amount of a mixture of two acids - methylindolylacrylic (see Experiment 1) and the original methylskatolidene malonic acid.

From the dimethylaniline layer was separated 1.2 g fine, silky needles with m.p. 70-73°, soluble in excess of hydrochloric acid and coming down again on addition of water. The solid was not soluble in the cold in water, ether, or ligroin, poorly soluble in benzene, and highly soluble in alcohol. It rapidly darkens in the air and becomes sticky. It rapidly resinifies when an attempt is made to wash it with water, and especially with ether.

It was only possible to obtain 0.1 g needles with a sandy color and m.p.

73-74° on recrystallization from benzene. After boiling for 2 hours with excess 10% potassium hydroxide solution, crystals with m.p. 98-99° were obtained which did not change even when exposed to the air for a long period. Owing to the small quantity, this substance was not investigated in more detail.

Analysis of substance with m.p. 73-74°:

4.537 mg substance: 13.288 mg CO_2; 3.432 mg H_2O.
7.897 mg substance: 21.724 mg CO_2; 5.486 mg H_2O.
Found %: C 84.27, 84.05; H 8.51, 8.71.
$C_{11}H_{11}N$. Computed %: C 84.04; H 7.05.

3. 2-Methylindole-3-aldehyde. A few experiments were performed with varying ratios of components for various periods of time. The reaction mixture acquired a bright cherry-red color on heating. Substantially the whole of the aldehyde was recovered in all of the experiments.

4. 1,2-Dimethylindole-3-aldehyde. Four experiments were carried out with differing ammonia concentrations, times of heating and ratios of starting materials. The same result was obtained in all of the cases. The main bulk of aldehyde was recovered unchanged and a negligible amount of a mixture of two acidic substances was isolated. The following is a description of one of the experiments.

A mixture of 5.9 g aldehyde, 4 g malonic acid, and 12 ml 10% ammonia solution was heated for 3 hours. The reaction mass acquired a cherry color. 4.1 g aldehyde with m.p. 126-128° was recovered unchanged from the soda-insoluble solid. On treating the alcoholic filtrate a further 1.3 g aldehyde was separated together with 0.2 g of a bright yellow substance melting at 133-150°.

Thus, 5.4 g aldehyde out of an original amount of 5.9 g was recovered.

Two compounds were isolated from the yellow solid by short boiling with benzene:

1) A white, benzene-soluble substance with m.p. 156-159° (I), and

2) A bright-yellow, benzene-insoluble compound with m.p. 154-156° (II).

Owing to the negligible amount of both of the substances, it was only possible to determine their acid values (using the combined products of all of the experiments).

0.1204 g substance (I): used 5.8 ml 0.1 N NaOH.
Equivalent found: 208.0.
$C_{13}H_{13}O_2N$ (dimethylindolyl-3-acrylic acid): computed equivalent 215.2
0.1080 g substance (II): used 8.0 ml 0.1 N NaOH.
Equivalent found: 135.0.
$C_{14}H_{13}O_4N$ (dimethylskatolidene malonic acid): computed equivalent 129.6.

III. Condensation of Indolealdehydes with Malonic Acid in Pyridine with Piperidine as Catalyst

A mixture of aldehyde, malonic acid, pyridine and piperidine was heated for 40 hours at a water bath temperature of 38-40°. A molar ratio of about 1:3 was taken in all of the cases for the aldehyde and malonic acid. The amount of pyridine was the minimum necessary for solution of the reacting components. The relative proportion of piperidine was the same in all of the experiments. The pyridine was first dried by standing for a long period over solid potassium hydroxide and then distilled.

1. Indole-3-aldehyde. A mixture of aldehyde (1.5 g), malonic acid (3.0 g)

pyridine (5 ml) and 5 drops piperidine was heated for 40 hours at a bath temperature of 38-40°. The reaction mass was poured into 300 ml water which had been acidified with hydrochloric acid and allowed to stand for 6 hours. The precipitate was separated from the liquid. The filtrate was made alkaline, freed from pyridine by extraction with ether, then acidified with hydrochloric acid and left till the next day. The precipitate was combined with the main bulk of previously separated solid (total 1.2 g) and worked up with 10% soda to give 0.3 g soda-insoluble material which after recrystallization did not depress the m.p. of the original aldehyde.

The soda filtrate was acidified with hydrochloric acid to give a dark-brown precipitate of β-(indolyl-3)-acrylic acid which, after recrystallization from water, melted at 194-195° (the literature [5] gives 195-196°). Yield 0.6 g, or 31.6% of theory, allowing for the unreacted aldehyde.

2. 1-Methylindole-3-aldehyde. 1.6 g aldehyde, 3.1 g malonic acid, 5 ml pyridine, and 5 drops piperidine were heated under the same conditions as above. The reaction mass was poured into 200 ml water when a yellow precipitate was at once formed and rapidly changed to an emerald color on standing in the air. The material was worked up as in the case of indole-3-aldehyde. Total yield was 2.1 g unrecrystallized solid and 0.3 g aldehyde was recovered.

Two fractions were separated from the soda filtrate, following the treatment of the yellow solid with soda solution, by fractional precipitation with dilute hydrochloric acid.

The first fraction, with a pale yellow color, weighed 0.4 g and had m.p. 130-135°; it was precipitated when the reaction was faintly alkaline to litmus. After reprecipitation and recrystallization from alcohol, there was obtained 0.2 g of white needles melting at 163°, and not depressing the m.p. of β-(1-methylindolyl-3)acrylic acid, prepared by decarboxylation of 1-methylskatolidene malonic acid in methylaniline.

The second fraction of 1.1 g, with a bright yellow color and m.p. starting at 165°, came down when the reaction to litmus was acid. Reprecipitation and recrystallization yielded 0.7 g green crystals melting with decomposition at 182-183° and not depressing the m.p. of 1-methylskatolidene malonic acid prepared from 1-methylindole-3-aldehyde and malonic acid under the conditions of Rodionov's reaction.

Consequently, 1.6 g aldehyde had yielded 0.7 g 1-methylskatolidene malonic acid and 0.2 g β-(1-methylindolyl-3)-acrylic acid. On the basis of the dicarboxylic acid the yield is 50% of the theoretical.

3. 2-Methylindole-3-aldehyde and 1,2-dimethylindole-3-aldehyde. Condensations were performed under the same conditions as for the preceding aldehydes. The reaction masses turned red during heating. Nearly the whole of the original aldehydes were recovered on working up and traces of substances with an acidic character were isolated but not further investigated.

IV. Condensation of Indolealdehydes with Ethyl Cyanoacetate.

To an alcoholic solution of aldehyde was added an alcoholic solution of ethyl cyanoacetate and piperidine. The mixture was left for two days at room temperature. The separated product of condensation was filtered at the pump and after one recrystallization was perfectly pure. The molar ratio of aldehyde and ethyl cyanoacetate in all of the experiments was about 1:1.5.

1. Indole-3-aldehyde. The reactants comprised 0.75 g aldehyde and 0.85 g ethyl cyanoacetate together with 18 ml alcohol and 3 drops piperidine. Considerable precipitation commenced after only an hour. After standing 48 hours, 1.15 g of the ethyl ester of α-cyano-β-indolylacrylic acid had separated out; m.p. 160-

162°; yield 91.9% of the theoretical. The product melted at 165° after recrystallization from alcohol. Van-Order and Lindwall [7] report a yield of 94% and m.p. 165°.

2. 1-Methylindole-3-aldehyde. Materials used were 0.5 g aldehyde, 0.5 g ethyl cyanoacetate, 12 ml alcohol, and 2 drops piperidine. As in the preceding experiment, precipitation commenced after an hour. There was obtained 0.7 g with m.p. 144-146°, corresponding to 93.7% of theory. The m.p. was 149-150° after one recrystallization from alcohol. M.p. 150° and a yield of 94% are reported in the literature [7] for the preparation obtained when using diethylamine as catalyst.

3. 2-Methylindole-3-aldehyde. Materials used were 0.6 g aldehyde, 0.5 g ethyl cyanoacetate, 10 ml alcohol, and 2 drops piperidine. Precipitation only occurred after 3 hours and in all 0.25 g product melting at 238-240° (with decomposition) was obtained. The yield was 26.3% of the theoretical on the basis of the ethyl ester of α-cyano-β-(2-methylindolyl-3)-acrylic acid. M.p. after recrystallization 239-240°. (The literature [10] records a m.p. of 246°).

0.4 g of unreacted aldehyde was recovered from the alcoholic filtrate by acidification with dilute acetic acid.

4. 1,2-Dimethylindole-3-aldehyde. Materials used were 1.5 g aldehyde, 1.5 g ethyl cyanoacetate, 34 mm alcohol, 5 drops piperidine. Precipitation only commenced after 30 hours. There was obtained 0.8 g yellow needles with m.p. 125-127°. The yield was 37.7% calculated on the ethyl ester of α-cyano-β-(1,2-dimethylindolyl-3)-acrylic acid. M.p. after recrystallization from alcohol 129-130°. 0.5 g unreacted aldehyde was recovered.

3.90 mg substance: 10.23 mg CO_2; 2.17 mg H_2O.
3.53 mg substance: 9.28 mg CO_2; 1.93 mg H_2O.
Found %: C 71.54, 71.70; H 6.22, 6.11.
$C_{18}H_{16}O_2N_2$. Computed %: C 71.62; H 5.97.

3.10 mg substance: 0.232 ml N_2 (22°, 736 mm).
3.01 mg substance: 0.215 ml N_2 (22°, 743 mm).
Found %: N 10.41, 10.22.
$C_{18}H_{16}O_2N_2$. Computed %: N 10.44.

SUMMARY

1. It was established that Rodionov's method for preparation of β-amino acids – condensation of aldehydes with malonic acid in alcoholic ammonia – was unsuitable for the synthesis of β-amino acids of the indole series. Condensation gives α,β-unsaturated acids.

2. The effect of the presence and position of the methyl groups on the condensing ability of indolealdehydes was determined. A methyl group at the second carbon atom reduces the ability of the aldehyde to condense, and a methyl group attached to the nitrogen atom increases it.

3. The rule in question was substantially confirmed in the condensation of these aldehydes with malonic acid by Döbner's method, as well as in their condensation with ethyl cyanoacetate.

LITERATURE CITED

[1] V.M.Rodionov and E.F.Malevinskaya, Ber., 59, 2952 (1926); V.M.Rodionov and A.M.Fedorova, Ber., 60, 804 (1927); Arch. Pharm. 266, 116 (1928); J.Am. Chem.Soc. 52, 368 (1930); V.M.Rodionov and E.A.Postovskaya, J.Am.Chem.Soc., 51, 841 (1929); V.M.Rodionov and E.I.Chukhina, J.Gen.Chem. 14, 325 (1944).

[2] V.M.Rodionov and V.K.Zvorykina, Bull.Acad.Sci.USSR, Div.Chem.Sci.,

217 (1943).

[3] German Patent 614, 325 (1929); Frdl., 22, 335.

[4] Mannich and Ganz, Ber., 55, 3487 (1922).

[5] Bauquess and Berg, J. Biol. Chem., 104, 675 (1934).

[6] Majima and Kotake, Ber., 58, 2037 (1925).

[7] R.Van-Order and H.Lindwall, J.Org.Chem. 10, 128 (1945).

[8] E.Restelli, Chem. Abs., 30, 1054 (1936).

[9] Majima and Kotake, Ber., 55, 3859 (1922).

[10] R.Seca, Ber., 57, 1868 (1924).

[11] W.Boyd and Robson, Biochem. J., 29, 551 (1935).

[12] German Patent 238,138 (1911); Frdl. 10, 332.

[13] Wieland, Konz, Mittasch, Ann., 513, 23 (1934).

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THE RELATIVE ACTIVITY OF METHYL KETONES

1. COLORIMETRIC INVESTIGATION OF THE REACTIVITY OF ACETONE AND ACETOPHENONE IN REACTIONS WITH 2-FURALDEHYDE

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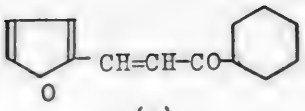
Variations may occur in the reactivity of a given organic compound in different reactions. A very interesting subject for investigation is therefore the comparative reactivity of a series of organic compounds with one other substance. In such cases the possibility presents itself of determining the components of mixtures consecutively by one and the same reaction without separation of the components of the mixture. A considerable simplification should then be effected in the procedure for analysis of organic compounds.

The comparative reactivity of ketones has been studied by several authors in respect of the formation of hydrazones, oximes, semicarbazones and bisulfite compounds (Petrenko-Kritchenko [1], Stewart [2], Conant and Bartlett [3], and others). The relative activity of ketones in condensations with aldehydes has hitherto received little attention. These reactions have been studied more closely in connection with aldehydes [4]. Investigations of the reactivity of ketones in the foregoing reactions naturally involved the determination of the concentration of ketone used in the reaction or formed during the condensation. The known reactions for determination of individual methyl ketones are few in number and relate to the colorimetric determination of only two ketones – acetone and acetophenone. However, the determination of ketone concentrations by other methods (gravimetric or volumetric) is extremely difficult; all of the other methods are general for all methyl ketones or ketones of all types or even for carbonyl compounds in general.

Our investigation concerns the problems of the relative activity of methyl ketones and the processes of their condensation with one aldehyde. We used 2-furaldehyde as the aldehyde in the reaction. Colorimetric determination was selected as the investigational method. The determination of the relative reactivity can be carried out by comparing the magnitudes of the velocity constants of these reactions [5]. It was impossible, however, to apply this method under our conditions, since, with excess of aldehyde, the order of the reaction of acetone with 2-furaldehyde differs from that of acetophenone with 2-furaldehyde.

Acetone and acetophenone react differently with 2-furaldehyde in an alkaline medium. Acetophenone yields only a single product – β-2-furylacrylophenone.

Three reaction products are formed in the condensation of equimolar quantities of acetone and 2-furaldehyde: 4-furyl-3-buten-2-one (II), 1,5-difuryl-3-pentadienone (III), and furyl-diacetone (IV).



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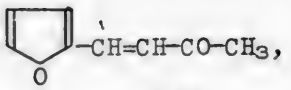

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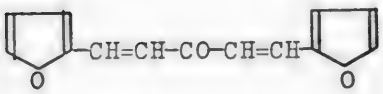

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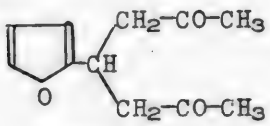

(IV)

(II) and (IV) are formed with excess of acetone. A single product of reaction is only formed when the 2-furaldehyde is in excess, the product then being 1,5-difuryl-3-pentadienone (III). A change in the concentration of compounds under these conditions (excess of 2-furaldehyde) only influences the reaction velocity without changing its character. In our investigation we therefore retained an excess of 2-furaldehyde in the reactions of these ketones with 2-furaldehyde.

We determined the relative activity of the ketones in the reaction with 2-furaldehyde by reference to the period of time from the start of the reaction to its conclusion, i.e., till the instant of establishment of equilibrium. The instant at which equilibrium is established between the forward reaction and the hydrolysis of the reaction products is naturally considered to be the end of the reaction between the 2-furaldehyde and the ketone. Consequently, at that instant the intensity of color of the reaction products must be a maximum.

The duration of the reaction, i.e., the length of time from the start of the reaction to its end (to the instant of equilibrium) may serve as a criterion of the relative activities of the ketones in their reaction with 2-furaldehyde. It should be remembered that the length of time from start to finish of the reaction is inversely proportional to the aldehyde concentration [6]. For this reason the 2-furaldehyde concentration was kept constant in all of the condensation experiments with use of various molar ratios of aldehyde to ketone. The change in concentration of the ketone is directly proportional to the intensity of the color, while the duration of the reaction does not change [7].

EXPERIMENTAL

Acetone and acetophenone were brought into reaction with 2-furaldehyde under identical conditions. The reaction took place in an alkaline medium at a definite concentration of catalyst and at constant temperature. The reaction components and the solvent were previously purified.

a) Condensation of 2-Furaldehyde with Acetone

Reaction was effected between equal volumes of 0.010 molar aqueous 2-furaldehyde, 0.004 molar alcoholic solution of acetone, and a 60% aqueous solution of potassium hydroxide at 20°. At the end of definite intervals of time, 2 ml samples of reaction mixture were withdrawn and dissolved in 20 ml of 50% sulfuric acid. The resultant red-colored acid solutions were analyzed in the photocolorimeter. The termination of the reaction was fixed as the maximum deviation of the galvanometer pointer from 100.

The results of colorimetric determinations are given in Table 1.

Examination of the data of Table 1 shows that the reaction of 2-furaldehyde

TABLE 1

Duration of Reaction of Acetone with 2-Furaldehyde

		Time (in minutes) from start of reaction						
		3	6	9	12	15	18	20
Galvanometer reading	1	63.0	54.8	52.5	51.4	50.0	51.0	51.0
	2	63.2	54.7	52.5	51.2	50.0	51.0	51.3
	3	63.2	54.6	52.6	51.5	50.1	50.8	51.4
Mean		63.1	54.7	52.5	51.4	50.0	50.9	51.2

with acetone under our conditions is completed within 15 minutes after its start.

Similar experiments were carried out with acetone in half the previous concentration while the concentrations of the other components remained unchanged.

Results of the determinations are given in Table 2.

TABLE 2

Duration of Reaction of Acetone with 2-Furaldehyde
(Ketone Concentration Halved)

		Time (in minutes) from start of reaction						
		3	6	9	12	15	18	20
Galvanometer reading	1	75.5	63.5	59.4	56.5	55.5	56.5	56.0
	2	75.2	63.5	59.5	56.5	55.6	56.8	56.0
	3	75.2	63.5	59.5	56.4	55.4	56.8	56.0
Mean		75.3	63.5	59.5	56.5	55.5	56.7	56.0

A comparison of the data of Tables 1 and 2 illustrates the lack of influence of the acetone concentration on the duration of the reaction, the only change being in the intensity of the color. Here also the reaction is completed within 15 minutes.

In order to establish the effect of change in the 2-furaldehyde concentration on the duration of the condensation process, we halved the concentration of 2-furaldehyde (to 0.005 molar), without changing the acetone concentration, which remained at 0.002 molar as in the second experiment.

Results are presented in Table 3.

TABLE 3

Duration of Reaction of Acetone with 2-Furaldehyde with Reduction in the Concentration of 2-Furaldehyde

		Time (in minutes) from start of reaction								
		9	12	15	18	20	25	30	35	40
Galvanometer reading	1	74.8	69.0	66.2	63.8	62.8	61.0	58.5	58.8	58.8
	2	74.5	68.9	66.2	63.8	62.8	60.8	58.4	58.4	58.6
	3	74.5	68.8	66.2	63.8	62.8	60.6	58.3	58.7	58.7
Mean		74.6	68.9	66.2	63.8	62.8	60.8	58.5	58.5	58.7

We see from the data in Tables 2 and 3 that when the 2-furaldehyde concentration is halved the duration of the condensation is doubled.

In all of these experiments the 2-furaldehyde remained in excess in relation to the acetone concentration in order to ensure that only one condensation product, 1,5-difuryl-3-pentadienone, would be formed during the condensation.

b) Condensation of 2-Furaldehyde with Acetophenone

The reaction of 2-furaldehyde with acetophenone was effected under conditions identical with those for the acetone reaction. An alkaline medium was used, samples of the reaction mixture were dissolved in ten times their volume of 50% sulfuric acid, and measurements were made in the photocolorimeter.

The components in the first experiment were equal volumes of 0.010 molar 2-furaldehyde solution, an alcoholic solution of acetophenone with a concentration of 0.004 molar, and a 60% aqueous solution of potassium hydroxide.

Results of determinations of the duration of the condensation are given in Table 4.

TABLE 4

Duration of Reaction of Acetophenone with 2-Furaldehyde

	Time (in minutes) from start of reaction								
	3	6	9	12	15	18	20	22	25
Galvanometer reading 1	91.2	86.5	84.0	82.0	81.4	80.7	80.5	80.4	80.8
Galvanometer reading 2	91.2	86.5	83.8	81.8	81.2	80.8	80.6	80.3	80.6
Galvanometer reading 3	91.2	86.5	83.6	81.8	81.2	80.9	80.4	80.2	80.5
Mean	91.2	86.5	83.8	81.8	81.2	80.8	80.5	80.3	80.6

In the next experiment the concentrations of both the ketone and the aldehyde were halved. The results are given in Table 5.

TABLE 5

Duration of Reaction of Acetophenone with 2-Furaldehyde with Reduced Concentrations of Aldehyde and Ketone

	Time (in minutes) from start of reaction								
	15	20	25	30	35	40	43	45	50
Galvanometer reading 1	90.0	89.0	88.4	87.2	86.3	85.8	85.0	85.0	85.5
Galvanometer reading 2	89.8	88.5	88.2	87.2	86.4	85.8	85.2	85.1	85.6
Galvanometer reading 3	89.8	88.5	88.2	87.2	86.4	85.8	85.0	85.2	85.8
Mean	89.8	88.7	88.2	87.2	86.4	85.8	85.1	85.1	85.6

Comparison of Tables 4 and 5 shows that reduction in the concentration of the excess 2-furaldehyde is accompanied by a proportional increase in the length of time between the start of the reaction and the moment of equilibrium. Thus, the change in the acetophenone concentration does not affect the duration of the process, just as was the case with the acetone.

From the colorimetric measurements we obtained a period of 15 minutes for the period of condensation of acetone and a period of 22 minutes for acetophenone, using 0.010 molar concentration of 2-furaldehyde and 0.004 molar concentration of the ketone. Hence the relative acitivites of the ketones in question in this reaction may be expressed by the inverse ratio of the durations of condensation: acetone:acetophenone = 22:15 = 100:68.

The same activity ratio persists when acetone and acetophenone are condensed with 2-furaldehyde in other concentrations. On halving the concentrations of 2-furaldehyde and ketones (under the same conditions in respect of catalyst and temperature), the reaction periods were 30 minutes for acetone and 43 minutes for acetophenone. The relative activitity of the ketones at these concentrations is accordingly 43:30 = 100:70.

The ratio obtained is characteristic of the reactivities of acetone and acetophenone with 2-furaldehyde.

Since the reaction velocity is also dependent upon the catalyst concentration (alkali), it was of interest to establish whether or not the activity ratio was maintained with different concentrations of alkali. With this aim we carried out experiments in which the concentrations of aldehyde and ketone remained constant while using a 30% solution of potassium hydroxide in place of 60%, i.e., the alkali concentration was halved.

Reactions were carried out with a mixture of equal volumes of 0.010 molar aqueous solution of 2-furaldehyde, 0.004 molar alcoholic solutions of the ketones, and an aqueous solution of the alkali.

Results of the colorimetric measurements appear in Tables 6 and 7.

TABLE 6

Duration of Reaction of Acetone with 2-Furaldehyde

	Time (in minutes) from start of reaction						
	15	20	24	27	30	33	36
Galvanometer reading .. 1	61.0	53.8	50.0	47.0	44.8	44.8	44.8
2	61.0	53.5	49.5	46.3	44.5	44.5	44.9
3	60.5	53.3	49.0	46.0	44.5	44.8	45.0
Mean	60.8	53.5	49.5	46.4	44.6	44.7	44.9

Tables 6 and 7 show that under the given conditions the reaction with acetone is completed in 30 minutes and that with the acetophenone in 43 minutes. On comparing these figures with those for the corresponding reactions in presence of more concentrated alkali, we can conclude that the duration of the reaction is

TABLE 7

Duration of Reaction of Acetophenone with 2-Furaldehyde

	Time (in minutes) from start of reaction							
	20	25	30	35	40	43	45	50
Galvanometer reading 1	72.0	68.4	65.8	65.0	63.0	62.3	62.5	62.8
2	72.0	68.2	65.5	64.8	63.2	62.1	62.4	62.8
3	71.8	68.1	65.5	64.8	63.2	62.1	62.1	62.5
Mean	72.0	68.2	65.6	64.9	63.1	62.2	62.3	62.7

inversely proportional to the catalyst concentration. This agrees with the observations of E.K.Nikitina and I.I.Paul in their investigations of the velocity of the reaction of acetone with 2-furaldehyde, [7]. Experiments have shown, however, that the determined ratios of activity are maintained also at various concentrations of catalyst: acetone:acetophenone = 43:30 = 100:70.

SUMMARY

1. A colorimetric comparison was made of the reactivity of acetone and acetophenone in the reaction with 2-furaldehyde. The duration of these reactions from their commencement to the moment of maximum development of color of reaction products was compared.

2. These determinations showed that the activity of acetophenone is 70% of the activity of acetone.

LITERATURE CITED

[1] P.Petrenko-Kritchenko, Ber., 34, 1702 (1901); J.Russ.Chem.Soc. 35, 406 (1903); 35, 146 (1903); 38, 773 (1906); 36, 1505 (1904).

[2] A.W.Stewart, J.Chem.Soc., 87, 410 (1905); 87, 175 (1905); J. prak. Chem., 83, 194 (1911).

[3] Conant and Bartlett, J.Am.Chem.Soc., 54, 288 (1932).

[4] V.V.Chelintsev and E.K.Nikitin, J.Gen.Chem. 2, 224 (1932); 10, 1453 (1940); 3, 319 (1933).

[5] E.K.Nikitin, J.Gen.Chem. 7, 2264 (1937).

[6] V.V.Chelintsev and E.K.Nikitin, J.Gen.Chem. 4, 438 (1934).

[7] E.K.Nikitin and I.I.Paul, J.Appl. Chem. 9, 1711 (1936).

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INVESTIGATIONS IN THE FIELD OF POLYCYCLIC COMPOUNDS. XIII.

THE ABSORPTION SPECTRA OF ANTHRAPYRIDONE-ACRIDONE, ANTHRAQUINONE-ACRIDONE, ANTHRAPYRIDONE, AND SOME OF THEIR DERIVATIVES

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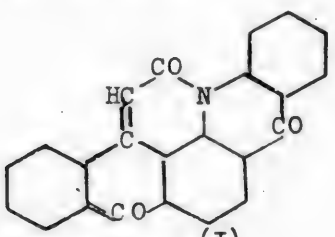
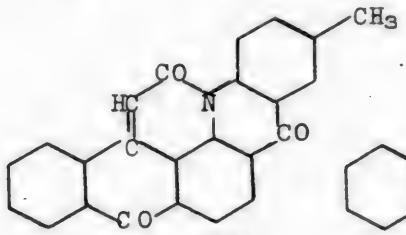
In previous communications, two of us have described the syntheses of anthrapyridone-acridone (I) [1], anthrapyridone-5"-methylacridone (II), and anthrapyridone-5",6"-benzacridone (III) [2], as well as the changes which take place in these compounds under the influence of aqueous alkali [3]. It was found that the action of a dilute solution of caustic soda on (I), (II), and (III) resulted in the rupture of their pyridine rings.

These phenomena were investigated in greater detail with compound (I), and it was found that the product of the reaction of (I) with caustic soda, obtained by the acidification of the alkaline solution, had the structure of anthrone-2,1-(N)-acridone-9-methylene-ω-carboxylic acid (IV).

In order to obtain a more complete characterization of the compounds enumerated, as well as additional confirmation of the correctness of the formula (IV) previously determined, we later carried out determinations of the absorption spectra of (I), (II), (III), and (IV), and compared them with the absorption spectra of anthraquinone-2,1(N)-acridone (V), N-methyl-1(N)-9-anthrapyridone (VI), and the methyl ester of n-phenyl-1(N)-9-anthrapyridone-2 carboxylic acid (VII).



(I)



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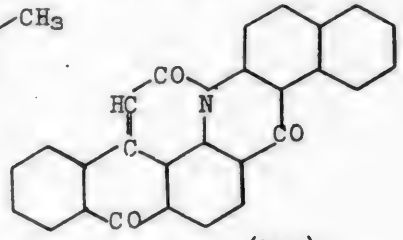

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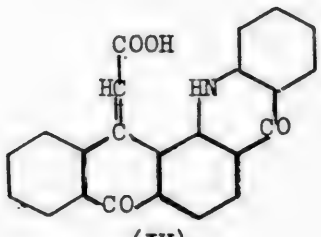
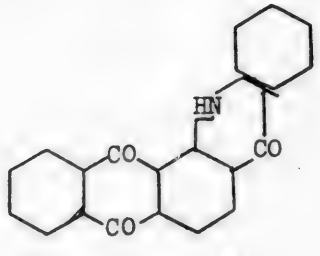
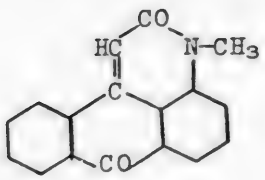


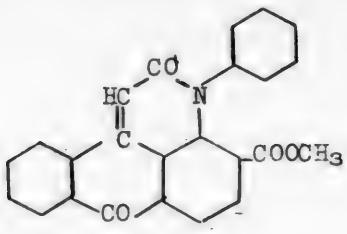
(IV)



(V)



(VI)



(VII)

As can be seen from Fig. 1, the absorption spectra of (I) and (II) are fairly close to each other, and differ chiefly by a small displacement of the positions of the maxima and in the intensity of the absorption.

Both substances show two definite maxima: (I) at 330 and 370 mμ, and (II) at 340 and 380 mμ. Anthrapyridone-benzacridone (III) has a completely different absorption curve. This is probably to be explained by the presence of an additional benzene nucleus.

In Fig. 2 are shown the absorp-

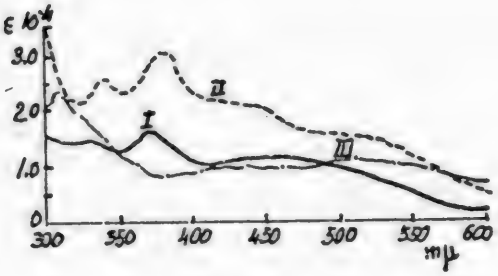


Fig. 1.

I) Anthrapyridone-acridone; II) anthrapyridone-5''-methylacridone; III) anthrapyridone-5'',6''-benzacridone

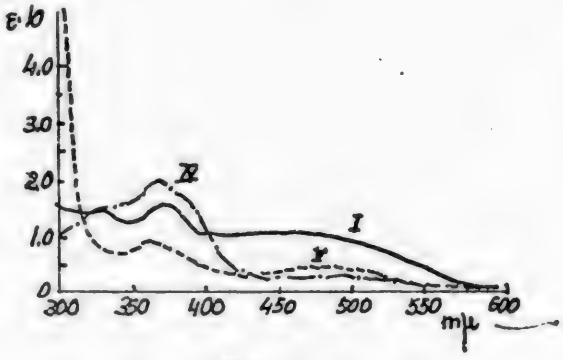


Fig. 2.

I) Anthrapyridone-acridone; IV) anthrone-2,1(N)-acridone-9-methylene carboxylic acid; V) anthraquinone-2,1(N)-acridone.

tion spectra of (IV) and (V). For the purpose of comparison, curve (I) is also given. All three compounds have an absorption maximum in a single region (365 to 370 mμ); this maximum is obviously characteristic for the anhtraquinone-acridone grouping. At the same time, curves (IV) and (V) do not show an absorption maximum at 330-340 mμ. This maximum has been observed in the case of all the compounds of the anthrapyridone series which we have investigated (except for (III).

In Fig. 3 are shown the absorption spectra of (VI) and (VII) along with the absorption spectrum of (II). As can be seen, the first maximum (at 340 mμ) coincides completely for all three compounds. In addition, (VI) has a second absorption maximum at 400 mμ and (VII) has one at 405 mμ.

The absence of a maximum at 340 mμ in the absorption spectrum of (IV) may be considered a confirmation of the structure previously determined by us, in accordance with which the product of the alkaline saponification of anthrapyridone-acridone lacks the pyridone grouping.

The measurements of the absorption spectra were carried out with a Beckmann spectrophotometer, model DU.

The measurements were carried out on solutions of the substances in 94% sulfuric acid.

The syntheses and properties of compounds (I), (II), (III), and (IV) have been previously described [1,2,3]; compounds (V) and (VI) were obtained according to the data in the literature [4,5]; and the synthesis and properties of (VII) are described below.

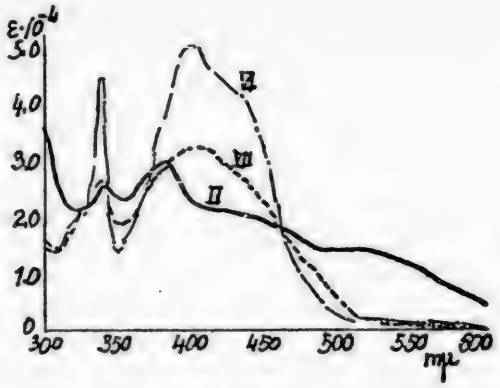


Fig. 3.

II) Anthrapyridone-5''-methylacridone; VI) N-methyl-1(N)-9-anthrapyridone; VII) N-phenyl-1(N)-anthrapyridone-2-carboxylic acid.

EXPERIMENTAL

The Methyl Ester of N-Phenyl-1(N),9-anthrapyridone-2-Carboxylic Acid (VII)

0.74 g of N-phenyl-1(N),9-anthrapyridone-2 carboxylic acid and 0.17 g of sodium bicarbonate were dissolved in 50 ml of water. The solution was filtered, and to it there was added 0.34 g of silver nitrate. The yellow-green precipitate which formed was filtered off, and washed with water and alcohol. The dried silver salt was mixed with 3 ml of methyl iodide, and boiled for 1.5 hours. The excess of methyl iodide was removed and the ester (VII) was extracted with 50 ml of benzene. There was obtained 0.37 g of light yellow needles.

After recrystallization from methyl alcohol and 50% acetic acid, the ester melted at 243-243.5°. It was soluble in most organic solvents. In concentrated sulfuric acid it formed a yellow solution which had a green fluorescence.

5.230 mg substance: 14.552 mg CO_2; 2.000 mg H_2O.
9.410 mg substance: 0.311 ml N_2 (23°, 755 mm).
Found %: C 75.93; H 4.28; N 3.79.
$C_{24}H_{15}O_4N$. Computed %: C 75.58; H 3.96; N 3.67.

SUMMARY

Measurements have been carried out on the absorption spectra of anthrapyridone acridone, anthrapyridone-5"-methylacridone, anthrapyridone-5",6"-benzacridone, anthrone-2,1(N)-acridone-9-methylene-ω-carboxylic acid, anthraquinone-2,1(N)-acridone, N-methyl-1(N),9-anthrapyridone, and the methyl ester of N-phenyl-1(N),9-anthrapyridone-2 carboxylic acid. The data obtained confirm the previously determined structure for compound (IV), which was obtained by the reaction of anthrapyridone-acridone with alkali.

LITERATURE CITED

[1] A.M.Lukin and P.M.Aronovich, J.Gen.Chem. 9, 1775 (1939).

[2] A.M.Lukin and P.M.Aronovich, J.Gen.Chem. 19, 358 (1949).*

[3] A.M.Lukin and P.A.Aronovich, J.Gen.Chem. 19, 362 (1949).**

[4] F.Ullmann and H.Bincer, Ber., 49, 732 (1916).

[5] German Patent 192,201, 1906; Frdl., 9, 732.

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* See CB translation p. 319 ff.
** See CB translation p. 323 ff.

THE TRANSFORMATION OF ASYMMETRICAL DIMETHYLDIPHENYLBUTINDIOL IN ACID MEDIUM

I. THE ISOMERIZATION OF THE GLYCOL UNDER THE INFLUENCE OF AN ALCOHOLIC SOLUTION OF SULFURIC ACID

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Among the many derivatives of acetylene, the acetylene γ-glycols have a special place. The investigation of this class of compounds, which is interesting in many respects, has considerable significance both for the solution of theoretical problems and for the synthesis of a number of compounds which are not without interest from the practical point of view.

In the course of our work on the investigation of the properties of asymmetrical dimethyldiphenylbutindiol (I) (2-methyl-5,5-diphenylpentin-3-diol-2,5), it became necessary to obtain the ethyl ester of this glycol.

The glycol itself is obtained easily and in good yield by the method of V.K.Teterin and A.P.Ivanov [1], by the action of benzophenone on the bromomagnesium alcoholate of the bromomagnesium derivative of dimethylacetylenyl carbinol [2], and is a crystalline substance with m.p. 116-117°.

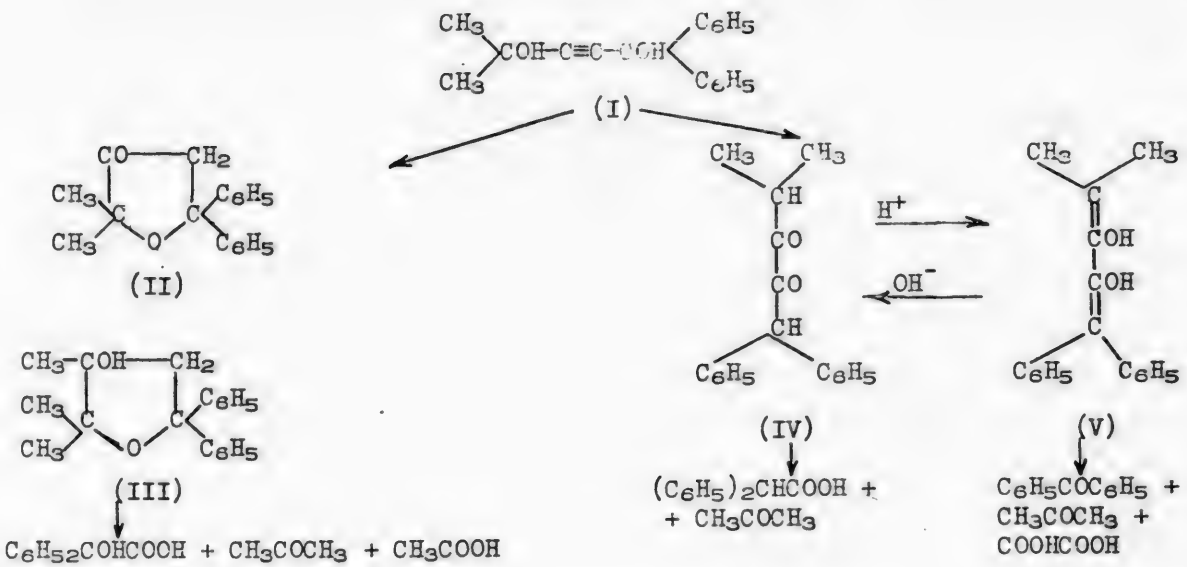
Whereas the Mamedov [3] method was used for the synthesis of the ethers of an entire series of acetylene γ-glycols of symmetrical structure, by means of heating solutions of the glycols in the corresponding alcohols in the presence of a small amount of sulfuric acid, we were unable to obtain so much as traces of the ethyl ether of the asymmetrical dimethyldiphenylbutindiol. The reaction took place in another direction, and we observed, that depending on the concentration of acid, there was an isomerization of the original glycol into a substituted tetrahydrofuranone and into an α-diketone with an open chain of carbon atoms.

Upon heating the glycol with an 18% alcoholic solution of sulfuric acid (by weight), we isolated in an amount 90% of that of the glycol used, colorless crystals of a compound isomeric with the glycol with m.p. 66-67°. This extremely readily formed a semicarbazone with m.p. 210°; it did not contain a hydroxyl group, and corresponded to 2,2-dimethyl-5,5-diphenyltetrahydrofuranone-3 (II).

In order to demonstrate the structure of the tetrahydrofuranone, it was transformed by means of a magnesium-organic synthesis into a tertiary alcohol of the tetrahydrofurane suries – 2,2,3-trimethyl-5,5-diphenyltetrahydrofuranol-3 (III), which was a colorless crystalline compound with m.p. 74-75° (Mechanism I).

Upon oxidation of the tetrahydrofuranol with potassium permanganate in the presence of caustic potash, there were obtained acetone, and acetic and benzilic acids. This confirmed the structure of this alcohol and the position of the hydroxyl group in the tetrahydrofurane ring, and consequently, the position of the keto group in tetrahydrofuranone (II).

Mechanism I



Similar tetrahydrofuranones were obtained by N.N.Nazarov [4] by the isomerization of unsaturated α-ketoacids.

Upon heating the asymmetrical dimethyldiphenylbutindiol with a 7.6% alcoholic solution of sulfuric acid, green crystals were obtained with m.p. 132-133°. These were also isomeric with the original γ-glycol, and were obtained in a yield above 90%, based on the amount of glycol.

This product, according to the analytical data, was an α-diketone with an open chain of carbon atoms – 2-methyl-5,5-diphenylpentandione-3,4 (IV). For the diketone we obtained a monosemicarbazone with m.p. 160-161° and a dioxime, which melted with decomposition in the range from 135 to 141° (Mechanism I).

An analogous rearrangement was observed in acid medium by V.N.Krestinsky [5] for tetramethylbutindiol, from which he was able to obtain both a colored diketone, and a colorless unsaturated α-ketoalcohol. In our case, in contrast to what Krestinsky observed, only the diketone was detected.

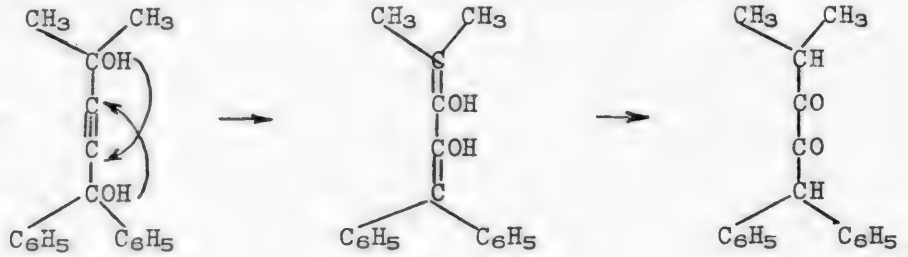
We must note the ease of transition of the α-diketone (IV) into the enol form (V). Upon oxidation with an aqueous solution of potassium permanganate at ordinary temperature, we observed among the products of oxidation acetone, benzophenone, and oxalic acid. These compounds could be obtained in case there was preliminary enolization of the diketone. In acid medium, oxidation took place with rupture of the molecule between the ketone groups, with the resultant formation of diphenylacetic acid and acetone as products of the further oxidation of isobutyric acid.

When 12.5% and 15.4% alcoholic solutions of sulfuric acid were used, a mixture of furanone and diketone was obtained. With the 12.5% sulfuric acid, the diketone predominated in the mixture, while with the 15.4% acid, the furanone predominated.

More concentrated sulfuric acid favored the isomerization of the glycol into the furanone, while with less concentrated acid the transformation of the glycol took place chiefly in the direction of the diketone.

The isomerization of the γ-glycol (I) and of the diketone (IV) probably takes place in the manner of the two-sided acetylene-allene rearrangement, with the formation of an intermediate dienol form (V) (Mechanism 2).

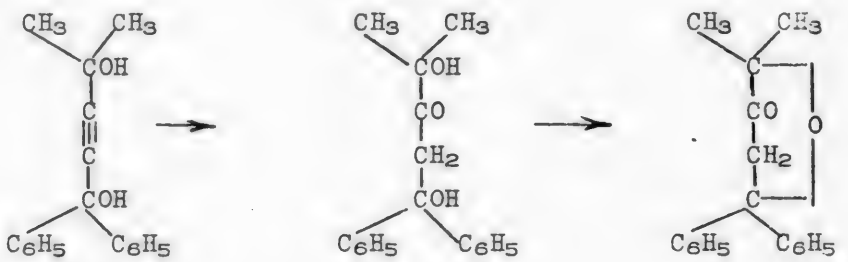
Mechanism 2



(I) (V) (IV)

In order to explain the formation of the furanone (II) from the γ-glycol, it is possible to assume the hydration of the triple bond of the glycol and the further cyclization of the unstable ketoglycol (VI), with the evolution of water (Mechanism 3).

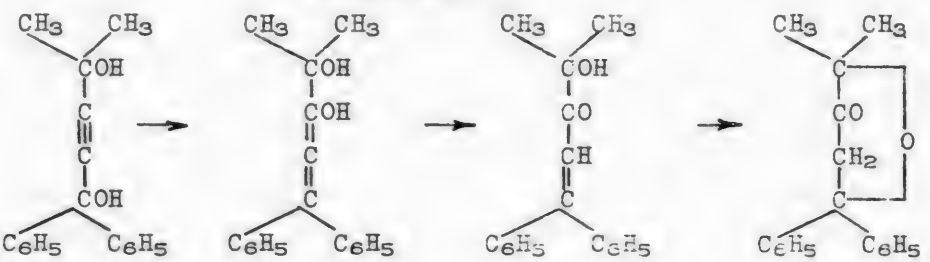
Mechanism 3



(I) (VI) (II)

The mechanism of the formation of the cyclic ketone (II) by way of the α-ketoalcohol of the ethylene series (VIII) is less probable in this case (Mechanism 4) as this ketoalcohol or its enol form (VII) was not observed by us at all, and in addition, in the case of this sort of mechanism, the isomerization of the γ-glycol would not be completely comprehensible, seeing that in less concentrated sulfuric acid the two-sided acetylene-allene rearrangement takes place with the formation of the diketone, while with more concentrated sulfuric acid the rearrangement is one-sided, and leads to the furanone, instead of the other way around.

Mechanism 4



(I) (VII) (VIII) (II)

A more thorough investigation of the transformation of asymmetrical dimethyldiphenylbutindiol will make it possible to give a more detailed analysis of the mechanism of its isomerization.

EXPERIMENTAL

The Transformation of Asymmetrical Dimethyldiphenylbutindiol Under the Influence of an Alcoholic Solution of Sulfuric Acid

Experiment I: 18% alcoholic solution of sulfuric acid.

To 80 ml of 95% ethyl alcohol there were added 7 ml of concentrated sulfuric acid (sp. gr. 1.83) and 10.5 g of the γ-glycol with m.p.116-117°. The mixture was heated on a water bath (60 to 70°) with stirring for 8 hours. After standing for a night, large well-shaped colorless crystals separated out. They had m.p. 66-67°, and were soluble in benzene, acetone, and ether. They crystallized excellently from alcohol in the form of large rhombic platelets. Yield 9 g, i.e., 85.7% of theory, based on the original glycol.

0.1400 g substance: 0.4155 g CO_2; 0.0873 g H_2O.
0.1328 g substance: 0.3946 g CO_2; 0.0818 g H_2O.
0.1022 g substance: 24.05 g C_6H_6: Δt 0.082°.
0.1083 g substance; 25.38 g C_6H_6: Δt 0.080°.
Found %: C 81.00, 81.08; H 6.93, 6.84; M 246, 270.
$C_{18}H_{18}O_2$. Computed %: C 81.20; H 6.76; M 266.

No hydroxyl groups were detected in the compound with m.p. 66-67°.

Preparation of the semicarbazone. To 0.5 g of the compound with m.p. 66-67° there were added 10 ml of alcohol and an excess of semicarbazide acetate in alcohol-water solution. The mixture was then heated on a water bath. As the temperature attained the melting point of the product (66-67°), the latter melted to form oily drops, which gradually dissolved, and there immediately began a voluminous separation of crystals of the semicarbazone. After recrystallization from alcohol, it melted at 210°.

0.1500 g substance: 16.8 ml N_2 (22°, 760 mm).
0.1145 g substance: 12.7 ml N_2 (20°, 764 mm).
0.1002 g substance: 0.2586 g CO_2; 0.0601 g H_2O.
Found %: C 70.39; H 6.66; N 12.95, 12.99.
$C_{18}H_{21}O_2N_3$. Computed %: C 70.59; H 6.50; N 13.00.

Preparation of the 2,2,3-trimethyl-5,5-diphenyltetrahydrofuranol-3 (III). For the reaction there were taken 0.9 g of magnesium, 6 g of methyl iodide, and 5 g of the tetrahydrofuranone. The methylmagnesium iodide was prepared in the usual way, and to it there was added drop by drop a solution of the ketone in 10 ml of absolute ether, the mixture being cooled and stirred. After all the ketone had been added, the mixture was stirred for an additional 36 hours at room temperature, and was then decomposed with moist ether, water containing ice, and dilute acetic acid. The ether extract was washed with a dilute solution of soda and water and dried with anhydrous sodium sulfate. Crystals precipitated out only after almost complete removal of the ether. They were in the form of very fine, small needles, which melted after recrystallization from ligroin at 74-75°. The compound was very soluble in alcohol, ether, acetone, ethyl acetate, and benzene, and somewhat less soluble in petroleum ether and ligroin. The yield was 90%, based on the original ketone.

0.1002 g substance: 0.2961 g CO_2; 0.0721 g H_2O.
0.1105 g substance: 0.3267 g CO_2; 0.0795 g H_2O.
Found %: C 80.59, 80.63; H 7.99, 7.99.
$C_{13}H_{22}O_2$. Computed %: C 80.85; H 7.80.

Determination of active hydrogen by the Chugaev-Tserevitinov method.

0.1082 g substance: 9.3 ml CH_4 (19°, 760 mm).
Found: 8.56 ml CH_4; % OH 5.34.
$C_{15}H_{21}O(OH)$. Computed: 8.59 ml CH_4: % OH 6.00.

Oxidation of the furane alcohol. A mixture of 2.2 g of the furane alcohol, 2.5 g of potassium permanganate, 0.8 g of potassium carbonate, and 125 ml of water was stirred for 20 hours at a bath temperature of about 85°. As the solution did not become colorless at the end, 1 ml of a 50% solution of caustic potash was added. After heating under the same conditions for an additional 10 hours the potassium permanganate was reduced.

The solution was filtered from the manganese dioxide, saturated with carbon dioxide, and the neutral products which were volatile with steam were driven off from it by heating. In the distillate, acetone was detected qualitatively by the iodoform test and the sodium nitroprusside test. The neutral products which were not volatile with steam were not separated. The alkaline solution which remained after the removal of the neutral products was dried on the water bath and treated with 10% sulfuric acid, which was added drop by drop until there was an acid reaction. The cloudy solution was extracted with ether to give colorless needle-shaped crystals, which gave a clear red color with concentrated sulfuric acid. After recrystallization from water, they melted at 149-150°, and did not give a depression of the melting point when mixed with benzilic acid [8].

From the acid solution, after the extraction of the benzilic acid, acetic acid was obtained by repeated extraction with ether. It was characterized by means of the silver salt:

0.1131 g salt: 0.0728 g Ag.
Found %: Ag 64.36.
$C_2H_3O_2Ag$. Computed %: Ag 64.66.

From manganese dioxide, distillation with steam gave a small amount of benzophenone, whose semicarbazone melted at 165-166°, and did not give a depression of the melting point with the known semicarbazone of benzophenone. In addition, the ether extracted 1.5 g of a substance with m.p. 75-76°, which did not give a depression of the melting point with the original alcohol.

The oxidation products of the alcohol were acetone, acetic and benzilic acids, as well as benzophenone, which was a product of the further oxidation of the benzilic acid. These confirmed the structure of the tetrahydrofurane alcohol (III) and the position of the alcohol group in the tetrahydrofurane ring, and this in turn confirmed the structure accepted by us for the furanone.

Experiment II: 7.6% alcoholic solution of sulfuric acid.

A mixture of 10 g of the glycol, 80 ml of ethyl alcohol, and 3 ml of concentrated sulfuric acid (sp. gr. 1.83) was heated for 6 hours on a water bath at 30-35°. The color of the solution gradually changed from light yellow to green. When the solution was cooled, there separated out, after several hours, sharply formed crystals in the shape of rectangular parallelopipeds with a yellow-green color. After recrystallization from alcohol, the substance melted at 132-133°. The yield was 90%, based on the original glycol.

The substance was soluble in benzene, ether, and acetone. It crystallized well from petroleum ether, forming crystals with a more pronounced yellow tinge than upon recrystallization from alcohol. The crystals were clumped together in nodules, and in a somewhat different form than when crystallized from alcohol.

0.1000 g substance: 0.2941 g CO_2; 0.0621 g H_2O.
0.1135 g substance: 20.32 g C_6H_6: Δt 0.106°.
0.1098 g substance: 19.06 g C_6H_6; Δt 0.110°.
Found %: C 81.10; H 6.90; M 269, 267.
$C_{18}H_{18}O_2$. Computed %: C 81.20; H 6.76; M 266.

The Chugaev-Tserevitinov reaction for the presence of active hydrogens was negative.

Preparation of the semicarbazone. To 2 g of the substance, 1.4 g of semicarbazide acetate was added in aqueous alcohol solution.

The mixture was subjected to long heating on the water bath, until the yellow-green color of the solution disappeared. Upon cooling, colorless, shining leaves precipitated out. After recrystallization from aqueous alcohol, these melted at 160°.

0.0971 g substance: 10.7 ml N_2 (18°, 760 mm).
0.0950 g substance: 0.2457 g CO_2; 0.0573 g H_2O.
Found %: C 70.39; H 6.70; N 12.80.
$C_{19}H_{21}O_2N_3$. Computed %: C 70.59; H 6.50; N 13.00.

Preparation of the dioxime. To a hot solution of 1 g of the compound in 10 ml of alcohol there were added 0.65 g of hydroxylamine hydrochloride and one drop of concentrated sulfuric acid. The mixture was heated with a reflux condenser for 20 hours on a boiling water bath. Upon cooling, it was diluted with water to a 50% alcohol content. After 4 days, colorless crystals separated out. After recrystallization from aqueous alcohol, these melted in the range from 135-141°, with decomposition.

0.0943 g substance: 0.2438 g CO_2; 0.0514 g H_2O.
0.0907 g substance: 7.5 ml N_2 (18°, 763 mm).
0.0506 g substance: 4.4 ml N_2 (22°, 758 mm).
Found %: C 73.31; H 6.29; N 9.73, 9.90.
$C_{18}H_{18}O_2N_2$. Computed %: C 73.48; H 6.13; N 9.56.

Oxidation of the compound with m.p. 132-133° with potassium permanganate. To a suspension of 2 g of the carfully extracted substance in 40 ml of water there was gradually added, while shaking by hand, as the decomposition progressed, 3.2 g of powdered potassium permanganate (based on a computation of 4 atoms of oxygen per one molecule of the original compound).

The colorless solution was filtered off from the manganese dioxide, which was treated with steam. From the cloudy distillate a yellow oil was extracted with ether. This crystallized after standing. After recrystallization from alcohol, the crystals melted at 47-49°, and did not give a depression of the melting point with benzophenone. After the treatment with steam, the manganese dioxide was extracted with ether; this gave 1 g of the original compound with m.p. 132°.

The aqueous alkaline filtrate from the manganese dioxide was saturated with carbon dioxide, and the acetone was then driven off by boiling and detected qualitatively.

The aqueous solution which remained after the distillation of the acetone contained salts of organic acids. It was acidified with dilute sulfuric acid and again distilled by itself to remove any organic acids which were volatile with steam. None were found.

The acid solution, which contained organic acids not volatile with steam, decolorized an aqueous solution of potassium permanganate upon heating, and after neutralization with ammonia gave with calcium chloride a precipitate which was insoluble in acetic acid.

The solution was placed in an extractor. After 40 hours of extraction with ether, colorless crystals appeared on the walls of the receiving vessel. After recrystallization from water they melted at 101-102°, and did not give a depression of the melting point when mixed with oxalic acid.

Oxidation of the compound with m.p. 132-133°, with chromic anhydride.

To a solution of 2.5 g of the compound in 25 ml of glacial acetic acid there was gradually added, with stirring and cooling, a solution of 2.5 g of chromic anhydride in 30 ml of acetic acid. After 24 hours, the oxidation was complete.

A part of the solution obtained was diluted to twice its volume with water, and the acetone was distilled off by boiling, and detected qualitatively after neutralization of the distillate. From the undiluted portion of the solution, acetic acid was distilled off under vacuum (b.p. 27-30° at 7-8 mm).

The residue from the distillation of the acetic acid was neutralized with soda and washed with water. Only 0.5 g of the original compound was detected in it.

The alkaline solution, obtained after washing the ether extract with soda, was acidified with dilute sulfuric acid, and from the cloudy solution a crystalline acid with m.p. 144-145° was extracted with ether. According to the data in the literature, diphenylacetic acid [7] melts at 146°. A mixture containing known diphenylacetic acid gave no depression of the melting point. The acid obtained was converted by means of its ammonium salt into the silver salt, which was analyzed.

0.1155 g salt: 0.0395 g Ag.
Found %: Ag 34.19.
$C_{14}H_{11}O_2Ag$. Computed %: Ag 33.90.

From the analytical data, the compound with m.p. 132° was an α-diketone isomeric with dimethyldiphenylbutindiol.

The results of the oxidation permit us to suggest that this diketone exists in the dienol form in alkaline medium.

Experiment III. 12.5% alcoholic solution of sulfuric acid.

In view of the fact that 18% sulfuric acid gave only the furanone and 7.6% acid only the diketone, in this experiment we used a 12.5% alcoholic solution of sulfuric acid.

5 g of the glycol, 40 ml of alcohol, and 2.5 ml of sulfuric acid (sp. gr. 1.83) were heated for 5 hours with stirring to 50°. The solution immediately acquired a yellow color. Upon cooling and standing, there was no precipitate from the solution. The solution was diluted with water, neutralized with soda, and extracted with ether. After the ether had been driven off, 4.6 g (92%) of fine yellow crystals were obtained. These melted at 130-132°. A mixed sample with the known diketone melted at 102-120°, which indicated the lack of homogeneity of the product.

Part of the substance obtained was recrystallized from alcohol, and another part from the petroleum ether. In both cases, fine yellowish green crystals with m.p. 132° quickly separated. These gave no depression of the melting point with the diketone. From the mother liquid there were obtained, upon standing, colorless, well-formed large crystals, slightly contaminated superficially with the yellow diketone. After washing with a small amount of cold petroleum ether, colorless crystals were obtained which melted at 66-67° and gave no depression of the melting point with the furanone.

In order to determine the amounts of furanone and diketone in the mixture obtained, we utilized the tendency of the furanone to give a semicarbazone quickly and quantitatively, in contrast to the diketone, whose monosemicarbazone formed very slowly and with difficulty.

From 1 g of the mixture of furanone and diketone obtained there was formed

a semicarbazone which, after removal from the yellow solution and recrystallization melted at 210° and did not give a depression of the melting point with the semicarbazone of the furanone.

The yield of semicarbazone was 0.42 g, which was computed to correspond to 0.3 g of the furanone. Consequently, 0.1 g of the mixture contained 0.3 g of the cyclic ketone and 0.7 g of the diketone. This meant that the glycol, on treatment with 12.5% sulfuric acid, was 30% isomerized into the furanone and 70% into the diketone.

Experiment IV: 15.4% alcoholic solution of sulfuric acid.

The experimental conditions were similar to those of the preceding experiment: the amounts of glycol and alcohol were the same, and 3 ml of sulfuric acid (sp. gr. 1.83) was used. The color of the solution was fainter than in Experiment III.

Almost 4.5 g of almost colorless crystals was obtained, part of which, after washing with cold petroleum ether and recrystallization from alcohol, melted at 66-67° and was in the form of large, colorless, well-formed, rhombohedra. A mixed sample with the known cyclic ketone did not give a depression of the melting point.

From the solution of petroleum ether there was obtained a very small amount of a yellow material which after recrystallization from boiling ligroin melted at 131-132.5° and corresponded to the diketone.

The semicarbazone with m.p. 210° was obtained in the amount of 1.2 g from 1 g of the original mixture of isomerization products. This showed that the mixture consisted to the extent of 85% of the furanone, and of 15% of the diketone.

SUMMARY

1. It has been found that asymmetrical dimethyldiphenylbutindiol (2-methyl-5,5-diphenylpentin-3,3-diol-2,5) does not form ethers with ethyl alcohol under the conditions in which such ethers are formed for a number of butindiols with symmetrical structure.

2. It has been shown that asymmetrical dimethyldiphenylbutindiol, under the action of an alcoholic solution of sulfuric acid, gives two isomeric substances:

a) A ketone of the tetrahydrofurane series – 2,2-dimethyl-5,5-diphenylfuranone-3, with m.p. 66-67°, upon heating to 60-70° with an 18% alcoholic solution of sulfuric acid;

b) An α-diketone with an open chain of carbon atoms – 2-methyl-5,5-diphenyl pentandione-3,4, with m.p. 131°, upon heating to 30-35° with a 7.6% alcoholic solution of sulfuric acid.

3). It has been shown that with alcoholic solutions of sulfuric acid of intermediate concentrations both the cyclic ketone and the diketone are formed, the ratios of these compounds in the mixture depending on the concentration of acid.

LITERATURE CITED

[1] V.K.Teterin and A.P.Ivanov, J.Gen.Chem. 7, 1629 (1937).
[2] Yu.S.Zalkind and A.P.Ivanov, J.Gen.Chem. 11, 803 (1941).
[3] Sh. Mamedov. Investigations in the Field of Glycol Ethers. Baku (1944).
[4] I.N.Nazarov, Bull. Acad. Sci. USSR, Div. Chem.Sci., 1, 107 (1948).
[5] V.N.Krestinsky and L.I.Bazhenova-Kozlovskaya, J.Gen.Chem. 2, 829 (1932).
[6] Beilstein, X, 342 (1926).
[7] Beilstein, IX, 673 (1926).

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THE TRANSFORMATION OF ASYMMETRICAL DIMETHYLDIPHENYLBUTINDIOL IN ACID MEDIUM

II. THE CONDENSATION OF THE GLYCOL WITH ETHYL ALCOHOL IN THE PRESENCE OF SULFURIC ACID

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In the first communication [1], a description was given of the isomeric transformations of the asymmetrical acetylenyl γ-glycol, 2-methyl-5,5-diphenylpentin-3-diol-2,5 (I) (asymmetrical dimethyldiphenylbutindiol) under the influence of an alcoholic solution of sulfuric acid on heating.

Upon heating the γ-acetylenyl glycol with an 18% alcoholic solution of sulfuric acid, we obtained 2,2-dimethyl-5,5-diphenyltetrahydrofuranone-3.

Upon more gentle heating of the glycol with a 7.6% alcoholic solution of sulfuric acid, the glycol was isomerized into an α-diketone, 2-methyl-5,5-diphenylpentanediol-3,4.

With alcoholic solutions of acid of intermediate concentrations, both substances were obtained.

Both these products of isomerization of the glycol were detected during an attempt to synthesize the ethyl ether of asymmetrical dimethyldiphenylbutindiol (I).

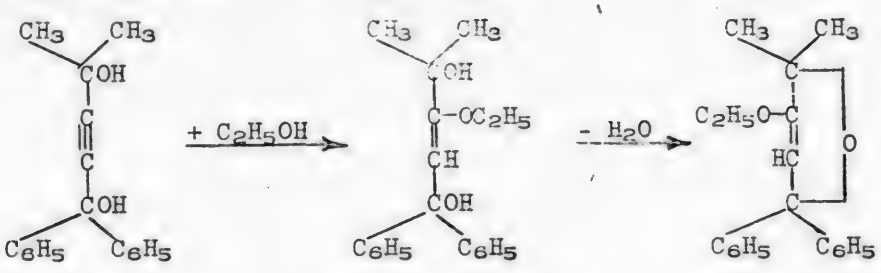
Not giving up the idea of obtaining the ethyl ether of this glycol, we decided to carry out the reaction under still milder conditions: with a very small amount of sulfuric acid (0.5% by weight) and almost no heating.

Under these conditions, there was obtained, along with the previously described [1] green crystals of the α-diketone, a second substance, which crystallized from petroleum ether in the form of well shaped colorless shining rectangular platelets with m.p. 64-65°.

The elementary analysis, molecular weight, and ethoxyl group content corresponded to the empirical formula of the ethyl monoether of dimethyldiphenylbutindiol. However, the substance we had obtained contained neither a hydroxyl group nor a triple bond. We could only assume that the addition of ethyl alcohol had taken place to the triple bond of dimethyldiphenylbutindiol, with subsequent dehydration and the formation of a substituted dihydrofurane – 2,2-dimethyl-5,5-diphenyl-3-ethoxydihydrofurane-2,5 (II). A similar addition reaction of phenol to tetraphenylbutindiol has been described by Yu.S. Zalkind, V.K. Teterin, and S.G. Kuznetsov [2].

Upon oxidation of this compound, an interesting characteristic came to light. The product obtained was stable, like many of the dihydrofurane derivatives, to oxidation in acid medium. But upon oxidation with an aqueous solution of potassium permanganate in the presence of caustic potash, a tendency to hydrolytic cleavage was observed at the position of the heteroatom, along with simultaneous

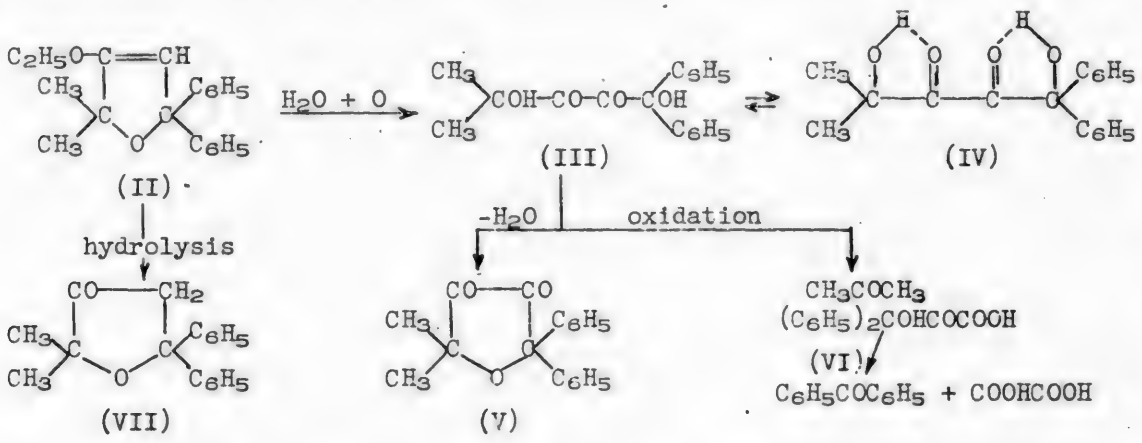
oxidation at the double bond of the ring.



(I) (II)

Among the neutral products of oxidation, a substance with m.p. 83-84° and the empirical formula $C_{18}H_{20}O_4$ was isolated. On the basis of its analysis, this could be assigned the structure of an α-diketo-γ-glycol – 2-methyl-5,5-diphenyl-pentandiol-2,5-one-3,4 (III).

In this substance the presence of two hydroxyl groups could be detected with difficulty, but it did not give the reactions customary for the carbonyl group. This might be explained by the presence of a hydrogen bond between the hydroxyls and the carbonyls which were present in α-positions with respect to each other (IV).



(II) (III) (IV) (VII) (V) (VI)

Upon heating the α-diketo-γ-glycol (III) with a 25% alcoholic solution of sulfuric acid, the dehydration of this substance took place, and a clear red, oily α-diketone of the tetrahydrofurane series (V) was obtained.

Similar sorts of diketones were obtained by Yu.S.Zalkind, V.K.Teterin, and S.G.Kuznetsov [2], as well as by T.I.Temnikova and P.A.Tikhomolov [3] as the result of the oxidation of tetraphenylbutindiol, its analogs, and its derivatives.

The structure of the α-diketone was shown by the formation of the corresponding quinoxaline upon reaction with o-phenylenediamine [4].

Upon oxidation of the α-diketo-γ-glycol (III), acetone and diphenylhydroxypyruvic acid (VI) were formed. Very few such acids have been described in the literature [5], and they have been comparatively little investigated. It has been noted that they are easily decarboxylated in the air, forming phenylhydrazones and semicarbazones, and upon oxidation break up into the corresponding ketones or aldehydes and oxalic acid.

The diphenylhydroxypyruvic acid obtained by us has not been described in the literature. It is a fairly viscous liquid, which with concentrated sulfuric

acid gives an intense blue color, and is decarboxylated in the air with extraordinary ease. The structure of the acid was shown by a complete analysis of its silver salt, and by the preparation and analysis of the corresponding semicarbazone. Further oxidation of the acid (VI) gave benzophenone and oxalic acid.

In order to demonstrate the position of the ethoxy group in the dihydrofurane ring, ethoxydihydrofurane (II) was heated with an 18% (by weight) alcoholic solution of sulfuric acid. As a result of hydrolysis, a crystalline product with m.p. 66-67° was obtained. This did not give a depression of the melting point with the known tetrahydrofuranone (VII), a product of the isomeric transformation of asymmetrical dimethyldiphenylbutindiol (I), described in the preceding communication. This conclusively confirmed for the substance (II) the structure 2,2-dimethyl-5,5-diphenyl-3-ethoxydihydrofurane-2,5.

The ethoxydihydrofurane contains a grouping peculiar to the vinyl ethers obtained by A.E.Favorsky and M.F.Shostakovsky by the action of alcohol on acetylene hydrocarbons in the presence of caustic potash [6].

The addition of alcohol to the triple bond of the acetylenyl γ-glycol in acid medium has been observed for the first time, and can serve as a confirmation of the mechanism of formation of the tetrahydrofurane suggested in the first communication [1], by means of the hydration of the triple bond of the γ-glycol, with subsequent cyclization.

EXPERIMENTAL

I. The Preparation of the Substituted Ethoxydihydrofurane, 2,2-Dimethyl-5,5-diphenyl-3-ethoxydihydrofurane-2,5 (II)

A mixture of 80 ml of ethyl alcohol, 10 g of asymmetrical dimethyldiphenylbutindiol, and 0.2 ml of concentrated sulfuric acid (0.5% alcoholic solution), was vigorously stirred, first at room temperature, and then with heating on a water bath at 30-35° for 20 hours. The solution was neutralized with soda and filtered. After 10 hours of standing, there separated from the solution a small amount of yellow-green crystals of the α-diketone, 2-methyl-5,5-diphenylpentandione-3,4, with m.p. 132°, described by us in communication I [1]. The crystals were filtered off, the alcohol driven off in vacuum, and the crystalline mass obtained was recrystallized from petroleum ether. Upon slow evaporation, the crystals of the α-diketone and the ethoxydihydrofurane (II) precipitated out separately, and they could be separated mechanically.

The colorless crystals were very soluble in alcohol, ether, acetone, and ethyl acetate; they crystallized well from petroleum ether. The m.p. was 64-65°, the yield 75%, computed on the basis of the original glycol used.

Analysis of the substance with m.p. 64-65°:

0.1002 g substance: 0.2987 g CO_2; 0.0685 g H_2O.
0.1230 g substance: 0.3667 g CO_2, 0.0841 g H_2O.
0.1415 g substance: 27.06 g benzene: Δt 0.09°.
0.1195 g substance: 29.83 g benzene: Δt 0.07°.
Found %: C 81.29, 81.30; H 7.59, 7.59; M 288, 294.
$C_{20}H_{22}O_2$. Computed %: C 81.60; H 7.50; M 294.

Determination of ethoxyl groups by Zeisel's method:

0.1684 g substance: 0.1318 g AgI.
0.1537 g substance: 0.1216 g AgI.
Found %: OC_2H_5 15.03, 15.20.
$C_{18}H_{17}O(OC_2H_5)$. Computed %. OC_2H_5 15.30.

2. The Oxidation of 2,2-Dimethyl-5,5-diphenyl-3-ethoxydihydrofurane-2,5

Preparation of 2,2-dimethyl-5,5-diphenylpentandiol-2,5-dione-3,4 (III). In a flask of 0.5 liter volume, there were placed 5 g of the ethoxydihydrofurane, a 2% aqueous solution containing 7 g of potassium permanganate, and 0.3 g of caustic potash. The mixture was heated, with energetic stirring, at a temperature from 70 to 80°.

After two days, the colorless solution of the alkaline salts of organic acids was filtered off from the manganese dioxide, and the neutral products insoluble in water. The latter had the appearance of a viscous mass, concentrated in the form of large greenish-yellow peas, which it was possible to separate from the manganese dioxide by means of a pointed glass rod. The manganese dioxide which remained was treated with steam. In the distillate, benzophenone was detected, and shown to be present by means of the semicarbazone.

The viscous mass of neutral oxidation products, to the amount of 4 g, was dissolved in ether, the solution was washed with water, and after the ether had been driven off, the residue was dissolved in 100 ml of boiling petroleum ether, from which there precipitated out, immediately upon cooling, greenish, plate-like crystals gathered together in nodules, to the amount of 2 g.

From the residue, after the removal of the petroleum ether, about 1.5 g of the original product was obtained.

The greenish products obtained from the neutral products of oxidation were recrystallized twice from petroleum ether. They then melted at 83-84°. The substance was very soluble in ether, benzene, and acetone, and somewhat less soluble in alcohol. It dissolved in petroleum ether only upon heating.

Analysis of the substance with m.p. 83-84°.

0.0792 g substance: 0.2110 g CO_2; 0.0438 g H_2O.
0.1000 g substance: 0.2660 g CO_2; 0.0563 g H_2O.
Found %: C 72.60, 72.70; H 6.10, 6.20.
$C_{18}H_{18}O_4$. Computed %: C 72.50; H 6.04.

Determination of the number of hydroxyl groups by the Terentyev method:

0.0376 g substance: 6.5 ml CH_4 (17°, 760 mm).
Found: 5.9 ml CH_4; % OH 11.80.
$C_{18}H_{16}O_2(OH)_2$. Computed: 5.7 ml CH_4; % OH 11.40.

Among the neutral products of oxidation which were volatile with steam, acetone was detected by the usual methods.

Preparation of the diketone of the furane series, 2,2-dimethyl-5,5-diphenyltetrahydrofurandione-3,4 (V). 0.35 g of the substance with m.p. 83-84°, 30 ml of alcohol, and 7 ml of concentrated sulfuric acid were heated with a reflux condenser for 2 hours. The solution acquired a clear raspberry color. A clear raspberry oil was extracted with petroleum ether, and after distillation of the solvent, the oil did not crystallize, and it was treated, without purification, with o-phenylenediamine.

Preparation of the quinoxaline. To an alcoholic solution of the clear raspberry-colored oil there were added an excess of o-phenylenediamine and an amount of concentrated hydrochloric acid equivalent to the diamine. The mixture was heated on a water bath until the raspberry color disappeared. Upon cooling, crystals separated out. After recrystallization from alcohol, these melted at 161-162°.

The quinoxaline crystallized from alcohol in the form of short rods with

hexagonal cross-sections and its faces strongly refracted light.

0.0424 g substance: 3.5 ml N_2 (21°, 753 mm).
Found %: N 8.00.
$C_{24}H_{20}N_2$. Computed %: N 8.50.

Preparation of diphenylhydroxypyruvic acid (VI). Diphenylhydroxypyruvic acid was obtained from the acid products of the oxidation of 2,2-dimethyl-5,5-diphenyl--3-ethoxydihydrofurane-2,5, upon acidifying the salts of the organic acids after the removal of the manganese dioxide and the neutral products of oxidation.

This was a liquid, oily substance, which with concentrated sulfuric acid gave an intense blue color which did not disappear upon long standing. The acid was decarboxylated even in the air, giving off bubbles of gas, which could be seen by the naked eye, and could be seen even better under the microscope.

The acid was converted, by the usual method, into the silver salt, upon which a complete analysis was carried out.

0.1172 g salt: 0.2119 g CO_2; 0.0334 g H_2O; 0.0350 g Ag.
0.1048 g salt: 0.1913 g CO_2; 0.0312 g H_2O; 0.0314 g Ag.
Found %: C 49.30, 48.80; H 3.15, 3.28; Ag 29.87, 29.86.
$C_{15}H_{11}O_4Ag$. Computed %: C 49.58; H 3.03; Ag 29.75.

The data obtained corresponded to those for diphenylhydroxypyruvic acid.

Preparation of the semicarbazone of diphenylhydroxypyruvic acid. About 0.5 g of the acid was dissolved in aqueous alcohol and mixed with an excess of an aqueous alcoholic solution of semicarbazone acetate. After 20 days of standing, crystals of the semicarbazone separated out. After recrystallization from alcohol, these melted with decomposition at 135°.

0.0526 g substance: 6.1 ml N_2 (15.5°, 756.5 mm).
Found %: N 13.55.
$C_{16}H_{15}O_4N_3$. Computed %: N 13.41.

The aqueous solution left after the extraction of the diphenylhydroxypyruvic acid was placed in a liquid extractor. Oxalic acid was extracted, and its identity shown by means of the calcium oxalate, and acetic acid was extracted and characterized by means of the silver salt.

Thus, the oxidation of 2,2-dimethyl-5,5-diphenyl-3-hydroxydihydrofurane-2,5, with m.p. 64-65°, gave, as neutral products: acetone, benzophenone, and the α-diketo-γ-glycol 2-methyl-5,5-diphenylpentandiol-2,5-dione-3,4; as acid products, acetic, oxalic, and diphenylhydroxypyruvic acids.

3. The Hydrolysis of 2,2-Dimethyl-5,5-diphenyl-3-ethoxydihydrofurane-2,5.

1 g of the compound, 8 ml of alcohol, 0.7 g of concentrated sulfuric acid, and 0.5 ml of water were heated on a water bath at 70-75° with constant stirring for 3 hours.

After the excess of alcohol had been driven off, there separated from the solution well-shaped crystals, identical with the 2,2-dimethyl-5,5-diphenyltetrahydrofuranone-3 described in communication I [1].

The identity of the products was shown by a mixed test and by the preparation of the semicarbazone with m.p. 210°, which did not give a depression of the melting point with the known semicarbazone of the tetrahydrofuranone.

SUMMARY

1. We have observed a tendency of the acetylenyl γ-glycol, 2-methyl-5,5-diphenylpentin-3-diol-2,5, to condense with ethyl alcohol in the presence of very

small amounts of sulfuric acid to give 2,2-dimethyl-5,5-diphenyl-3-ethoxydihydrofurane-2,5.

2. The 2,2-dimethyl-5,5-diphenyl-3-ethoxydihydrofurane-2,5 is hydrolyzed in acid medium with the formation of a ketone of the tetrahydrofurane series, 2,2-dimethyl-5,5-diphenylfuranone-3.

3. Upon oxidation in alkaline medium, the hydrolytic cleavage of the dihydrofurane ring of 2,2-dimethyl-5,5-diphenyl-3-ethoxydihydrofurane-2,5 takes place, with the formation of an α-diketo-γ-glycol, 2-methyl-5,5-diphenylpentandiol-2,5-one-3,4. Upon dehydration, this is converted into a diketone of the tetrahydrofurane series, 2,2-dimethyl-5,5-diphenyltetrahydrofurandione-3,4, and upon oxidation it gives diphenylhydroxypyruvic acid.

LITERATURE CITED

[1] Yu.S.Zalkind, E.D.Venus-Danilova, and V.I.Ryabtseva, J.Gen.Chem. 20, 2222 (1950).*

[2] Yu.S.Zalkind, V.K.Teterin, and S.G.Kuznetsov, J.Gen.Chem. 15, 488 (1945).

[3] T.I.Temnikova and P.A.Tikhomolov, J.Russ.Chem.Soc., 62, 1217 (1930).

[4] P.A.Tikhomolov and A.E.Druzhinin, J.Gen.Chem. 7, 869 (1937).

[5] E.Hoff and Chargaft, J. Biol. Chem., 164, 417 (1932); V.N.Krestinsky and L.I.Bazhenova-Kozlovskaya, J.Gen.Chem. 2, 236 (1932); Beilstein, X, 673 (1921).

[6] A.E.Favorsky and M.F.Shostakovsky, J.Gen.Chem. 13, 1 (1943).

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*See CB translation p. 2309 ff.

ON THE REACTION OF THE ESTERS OF CINNAMIC ACID WITH ISOPROPYLMAGNESIUM BROMIDE, ISOBUTYLMAGNESIUM IODIDE AND BROMIDE, n-BUTYLMAGNESIUM BROMIDE, AND PHENYLMAGNESIUM BROMIDE

A. D. Petrov and P. S. Bataev

In the investigations by one of the present authors [1] of a long series of acids of the type $-CH_2COOH$ (from butyric to palmitic, inclusive) as well as on the esters of benzoic acid, it was shown that there was another course for the magnesium-organic synthesis for tertiary and secondary MgR_1X_1, as compared with the primary compounds, namely, the formation, instead of tertiary alcohols, of symmetrical ketones containing radicals corresponding to the radical of the acid used. In continuing this investigation, A.D.Petrov recently showed [2] that the esters of such strong acids as formic and o-hydroxybenzoic also reacted with secondary alkyl-magnesium halides (isopropylmagnesium bromide) according to the nomral mechanism. It was of interest to investigate the relation with regard to the secondary alkyl-magnesium halide of the esters of acids containing a double bond in the α,β-position to the carboxyl, i.e., of the type of $-CH=CH-COOH$.

The literature contains [3] only investigations of the reactions of esters of cinnamic acid with the Grignard reagents CH_3MgBr and C_6H_5MgBr, which have no tendency to decompose (the first of these is added in the 1,2 position, the second in the 1,4.) Therefore it seems to us of interest to carry out a parallel investigation of the behavior in syntheses with the esters of cinnamic acid of the radicals: isopropyl, isobutyl, and n-butyl. These latter primary alkyl halides also frequently behave in a different manner with the esters of different acids. While, for example, $n\text{-}C_4H_9MgBr$, in all the cases investigated, reacts with the esters of monobasic acids in such a way as to lead invariably to the formation of only tertiary alcohols, $iso\text{-}C_4H_9MgBr$ reacts with the ester of benzoic acid, as has been shown by P.P.Shorygin [4], to give chiefly the secondary alcohol. Skraup and Freundlich [5] were unable to obtain the tertiary alcohol by the reaction of this alkyl halide with the ester of isovaleric acid, and Halse [6] obtained the tertiary alcohol (methyl-diisobutyl carbinol) only by reaction with the ester of a strong acid like acetic, which was also distinguished by its small steric hindrance. Among the products of the benzyl ester of cinnamic acid with isopropylmagnesium bromide we isolated dibenzal acetone. However, a great portion of the products of the reaction consisted of alcohols, including the tertiary, the latter giving as a product of dehydration diene hydrocarbons and tar.

In the case of n-butylmagnesium bromide and the benzyl ester of cinnamic acid, the reaction products consisted of the tertiary alcohol, styryldibutyl carbinol, mixed with benzyl alcohol, dienes and tar. Here there were no crystals. The

formation of the tertiary alcohol (i.e., the addition of n-C_4H_9MgBr in the 1-2 position) was confirmed by the reaction of n-butylmagnesium iodide also with the ethyl ester of cinnamic acid. In this latter case, the tertairy alcohol, which was obtained in a higher degree of purity, was dehydrated, and the hydrocarbon formed was oxidized. Among the products of oxidation, benzoic and butyric acids were identified. In the case of the benzyl ester of cinnamic acid, the reaction with isobutylmagnesium iodide took place chiefly according to the mechanism already indicated for n-butylmagnesium bromide, with the formation of the tertiary alcohol, dienes, and tar, that is, it differed from the reaction of this alkyl halide with the ester of benzoic acid. In addition, a crystalline reaction product, which turned out to be stilbene, was here formed. We cannot assume the formation of stilbene to be the result of the disproportionation of benzil, as this sort of disproportionation would also have to take place in the reaction with isopropyl bromide. There, however, no stilbene is formed. It appeared to us more probable that the formation of stilbene was the result of the condensation and decomposition of the magnesium halide-alcoholate of benzyl alcohol, according to the equations:

$$C_6H_5-CH=CH-\overset{\overset{O}{\|}}{C}-OCH_2C_6H_5 + IMg-CH_2-\underset{\displaystyle CH_3}{\underset{|}{CH}}-CH_3 \longrightarrow$$

$$\longrightarrow C_6H_5-CH=CH-CO-CH_2-\underset{\displaystyle CH_3}{\underset{|}{CH}}-CH_3 + C_6H_5CH_2-OMgI;$$

$$2C_6H_5-CH_2-OMgI \longrightarrow Mg(OH)I + C_6H_5CH(OMgI)-CH_2C_6H_5 \longrightarrow$$

$$\longrightarrow Mg(OH)I + C_6H_5-CH=CH-C_6H_5.$$

The formation of stilbene is probably to be explained not so much by the specific influence of the isobutyl radical as by the condensing action of the iodine. We may recall that in the reaction of cyclohexylmagnesium bromide with benzophenone, as A.E.Arbuzov and I.A.Arbuzova have shown, benzhydrol is formed, while the action of cyclohexylmagnesium iodide gives benzpinacone.

In the reaction of the benzyl ester of cinnamic acid with C_6H_5MgBr, when carried out at +20°, there is formed, if we do not count the benzyl alcohol, only the saturated tertiary alcohol 1,1,3,3,-tetraphenylpropyl alcohol, with m.p. 95°. This synthesis takes place, apparently, according to the following equations:

$$C_6H_5-CH=CH-\overset{\overset{O}{\|}}{C}-OCH_2C_6H_5 + C_6H_5MgBr \longrightarrow C_6H_5-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-CH=\overset{OMgBr}{\overset{|}{C}}-OCH_2-C_6H_5$$

$$C_6H_5-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-CH=\overset{OMgBr}{\overset{|}{C}}-OCH_2C_6H_5 + C_6H_5MgBr \longrightarrow C_6H_5-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-CH=\overset{OMgBr}{\overset{|}{C}}-C_6H_5 + C_6H_5CH_2OMgBr.$$

$$C_6H_5-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-CH=\overset{OMgBr}{\overset{|}{C}}-C_6H_5 + C_6H_5MgBr \longrightarrow C_6H_5-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-\underset{\displaystyle MgBr}{\underset{|}{CH}}-\overset{OMgBr}{\overset{|}{C}}=(C_6H_5)_2 \longrightarrow$$

$$\longrightarrow C_6H_5-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-CH_2-\overset{C_6H_5}{\overset{|}{C}}OH$$
$$\qquad\qquad\qquad

It is of interest to note that Kohler [8], in carrying out the synthesis with C_6H_5MgBr and the ester of cinnamic acid at -10°, obtained only the intermediate product of this synthesis: the ester of β,β-diphenylpropionic acid with m.p. 133°, and diphenylpropiophenone with m.p. 47°. Kohler [9] was able to obtain 1,1,3,3-tetraphenylpropyl alcohol only by the reaction of C_6H_5MgBr with benzalacetophenone. Thus, the halting of the reaction at intermediate stages may sometimes be the result not only of steric hindrance, but of a lowering of the reaction temperature.

EXPERIMENTAL

1. Isopropylmagnesium bromide and the benzyl ester of cinnamic acid.

We used 36 g of magnesium, 185 g of isopropyl bromide, and 225 g of the ester of cinnamic acid. After decomposition, there were obtained:

Fraction I, with b.p. 61.5° at 2mm, 58 g; Fraction II, with b.p. 90° at 1 mm, 7 g; and III, a tarry residue, 210 g.

Although the percent of hydroxyl groups found by analysis in Fraction I was close to that required for styrylisopropyl carbinol, and in Fraction II was close to that required for styryldiisopropyl carbinol, the data of elementary analysis, and the values of n_D^{20} and d_4^{20} indicated that in these fractions we had a complicated mixture of the alcohols indicated with benzyl alcohol and diene hydrocarbons, formed as a result of the dehydration of the tertiary alcohol.

From the tarry residue, which consisted chiefly of polymers of the diene hydrocarbons, we obtained in an amount of about 1.5 g lemon-yellow crystals with m.p. 112° (after recrystallization).

11.52 mg substance: 36.59 mg CO_2; 6.28 mg H_2O.
10.40 mg substance: 33.04 mg CO_2; 5.84 mg H_2O.
Found %: C 86.68, 86.83; H 6.10, 6.28.
$C_{17}H_{14}O$. Computed %: C 87.17; H 5.98.

Determination of molecular weight:

0.1332 g substance; 14.25 g benzene: Δt 0.199°.
Found: M 242.
$C_{17}H_{14}O$. Computed: M 234.

A mixed test with known dibenzal acetone showed no depression.

2. Isobutylmagnesium iodide and the benzyl ester of cinnamic acid.

We used 12 g of magnesium, 0.5 mole of isobutyl iodide, and 0.5 mole of the ester. Fractional distillation of the reaction product gave:

Fraction I, with boiling range 78-121.5° at 5 mm, 2 g; Fraction II, with boiling range 121.5-125° at 1 mm, 25 g; Fraction III, with boiling range 125-166° at 1 mm, 20 g, and IV, tarry residue, 65 g.

Determination of the number of hydroxyl groups, by Tserevitinov's method, on the fraction with range 121-125° at 1 mm:

0.2402 g substance: 23.4 ml (0°, 760 mm).
Found %: OH 7.44.
$C_{17}H_{26}O$. Computed %. OH 6.91.

d_4^{20} 0.9749; n_D^{20} 1.5251:

Found: MR_D 77.33.
$C_{17}H_{26}O$. Computed: MR_D 78.16.

It is obvious that despite the fact that the percentage of OH corresponds to

to that required, the fraction with boiling range 121-125° at 1 mm is, just as in the first experiment, a complicated mixture of products.

The fraction with boiling range 125-166° at 1 mm hardened completely to give a white mass. In trying to determine whether or not it contained the original ester, we saponified it with a 10% solution of caustic potash. After the saponification, crystals separated out with m.p. 124° (after recrystallization). These gave a dibromide with m.p. 237°.

The molecular weight was determined for the crystals with m.p. 124°;

0.0742 g substance; 16.31 g benzene: Δt 0.125°.
Found: M 186.6.
$C_{14}H_{12}$. Computed: M 180.1.

3. n-Butylmagnesium bromide and the benzyl ester of cinnamic acid, n-butylmagnesium iodide and the ethyl ester of cinnamic acid.

We took 48 g of magnesium, 280 g of n-butyl bromide, and 290 g of the benzyl ester of cinnamic acid. Upon decomposition, we obtained 52 g of a fraction with boiling range 129-132° and 180 g of a tarry residue.

The fraction obtained, according to the data of elementary analysis and the values of n_D^{20} and d_4^{20}, was a mixture of benzyl alcohol with a tertiary alcohol (styryl-dibutyl carbinol) and the products of the latter's dehydration.

Wishing to obtain a purer tertiary alcohol, we carried out a second synthesis with 36 g of magnesium, 285 g of n-butyl iodide, and 140 g of the ethyl ester of cinnamic acid. The first distillation gave: Fraction I, with boiling range up to 46° at 5 mm, 39.5 g; Fraction II, with boiling range of 46-140° at 5 mm, 5 g; Fraction III, with boiling range 140-176° at 3 mm, 48 g; Fraction IV, tarry residue, 95 g.

Upon a second fractionation of Fraction III in vacuum, there were obtained:

Fraction I with boiling range up to 120° at 1.5 mm, 2.6 g; Fraction II with boiling range 120-123.5° at 1.5 mm, 37.4 g; fraction III with boiling range 123-130° at 1.5 mm, 3.8 g. Residue, 3.5 g.

Fraction II, with boiling range 120-123.5° at 1.5 mm, 30 g in amount, was dehydrated over a Houdry catalyst in the apparatus of Dine and Stark. There were obtained 2.3 g of water and 17.5 g of a hydrocarbon with boiling range 130-140.3°, at 5 mm. The latter was oxidized with a 1% solution of $KMnO_4$. Among the products of oxidation, benzoic and butyric acids were identified.

4. Phenylmagnesium bromide and the benzyl ester of cinnamic acid.

We used 36 g of magnesium, 164 g of bromobenzene, and 0.5 mole of the ester of cinnamic acid. After decomposition, which took place with greater difficulty than usual, and for the accomplishment of which it was necessary to use a 3% solution of H_2SO_4, the reaction product was fractionally distilled to give: Fraction I with boiling range 46-89° at 9 mm, 13 g; Fraction II with boiling range 89-90° at 6 mm, 15 g; fraction III with boiling range 90-160° at 6 mm, 81 g; Fraction IV, tarry residue, 142 g.

Fraction II, with boiling point 89-90° at 6 mm, was distilled at atmospheric pressure at 202-204°. It was benzyl alcohol.

10.08 mg substance: 28.43 mg CO_2; 6.95 mg H_2O.
Found %: C 76.97; H 7.70.
C_7H_8O. Computed %: C 77.77; H 7.40.

d_4^{20} 1.0483; n_D^{20} 1.53803.

Found: MR_D 32.24.
C_7H_8O. Computed: MR_D 32.44.

Determination of the content of hydroxyl groups:

0.2254 g substance: 47.52 ml (0°, 760 mm).
Found %: OH 16.10.
C_7H_8O. Computed %: OH 15.74.

Fraction III crystallized, and after numerous recrystallizations from petroleum ether, had m.p. 94-95°, corresponding to that of 1,1,3,3-tetraphenylpropyl alcohol.

0.1620 g substance; 10.38 g benzene: Δ t 0.140°
Found: M 361.9.
$C_{27}H_{24}O$. Computed: M 364.

3.54 mg substance: 15.521 mg CO_2; 1.985 mg H_2O.
3.119 mg substance: 10.110 mg CO_2; 1.730 mg H_2O.
Found %: C 88.46, 88.46; H 6.25, 6.21.
$C_{27}H_{24}O$. Computed %: C 89.01; H 6.59.

Determination of hydroxyl groups by Tserevitinov's method:

0.1709 g substance: 10.37 ml (0°, 760 mm).
Found %: OH 4.64.
$C_{27}H_{24}O$. Computed %: OH 4.67.

The 13 g of the alcohol was subjected to lengthy hydrogenation (120 hours) over Raney nickel at a temperature of 180-220° and a pressure of from 200 to 260 atm. The main portion of the hydrogenated product (9 g) distilled over at 188-191° at 2 mm.

Determination of molecular weight:

0.5302 g substance; 19.21 g benzene; Δ t 0.499°.
0.1508 g substance: 18.31 g benzene; Δ t 0.144°.
Found: M 284.4, 293.6.
$C_{21}H_{38}$. Computed: M 290.

14.10 mg substance: 45.47 mg CO_2; 14.94 mg H_2O.
13.63 mg substance: 43.91 mg CO_2, 14.77 mg H_2O.
Found %: C 88.01, 87.80; H 11.85, 12.11.
$C_{21}H_{38}$. Computed %: C 86.90; H 13.10.

d_4^{20} 0.9359; n_D^{20} 1.5144.
Found: MR_D 93.345.
$C_{21}H_{38}$. Computed. MR_D 92.578.

From the data given, it can be seen that despite the partial cracking (cleavage of one ring, as a result of the harsh conditions and the great length of hydrogenation) we obtained 1,1,3-tricyclohexylpropane, still containing about 15% of 1,1,3-triphenylpropane. This mixture of hydrocarbons hardened to give a glass at a temperature of about -50°C.

SUMMARY

1. It has been shown that the reaction of the benzyl ester of cinnamic acid with n-butylmagnesium bromide gives a tertiary alcohol, styryldibutyl carbinol, which is partially dehydrated with the formation of diene hydrocarbons, which are converted into a tar.

2. Isobutylmagnesium bromide reacts with the same ester in similar fashion, the tertiary alcohol here being obtained in greater yield than in the reaction

of the isobutylmagnesium halide with the ester of benzoic acid. In addition, in this reaction it was noted that the iodine had a condensing action on the magnesium halide-alcoholate of benzyl alcohol, leading to the formation of stilbene.

3. Isopropylmagnesium bromide gives, with the ester of cinnamic acid, a small yield of dibenzalacetone, i.e., the reaction here takes place partially with the formation of a ketone of the type R–CO–R, according to the mechanism previously found for esters of acids like $-CH_2COOH$ and benzoic acid. At the same time the reaction also takes place here with higher yields according to the normal mechanism in the direction of the corresponding tertiary alcohol.

4. C_6H_5MgBr reacts with the ester of cinnamic acid when the synthesis is carried out at +20° to give only 1,1,3,3-tetraphenylpropyl alcohol. Upon hydrogenation of this alcohol, 1,1,3-tricyclohexylpropane was obtained (as a result of partial cracking).

LITERATURE CITED

[1] A.D.Petrov, K.I.Karasev, M.A.Cheltsova, J.Gen.Chem. 6, 522 (1936).

[2] A.D.Petrov, E.B.Sokolova, J.Gen.Chem. 8, 199 (1938); A.D.Petrov and A.Kukanova, J.Gen.Chem. 7, 2665 (1937) and others; A.D.Petrov, Proc.Acad.Sci. USSR, XIII, No. 1, 41 (1948).

[3] Runge, Magnesium-organic Compounds, 1937, p. 185.

[4] P.P.Shorygin, Ber., 40, 3111 (1907).

[5] Skraup and Freundlich, Ber., 55, 1075.

[6] Halse, J. prak. chem., (2) 89, 458.

[7] A.E.Arbuzov and I.A.Arbuzova, J.Gen.Chem. 2, 388 (1932).

[8] E.Kohler and G.Heritage, J.Am.Chem.Soc., XX, 21; J.Am.Chem.Soc., 31, 642.

[9] E.Kohler, Am. Chem. J., 33, 21 (1905).

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THE AROMATIZATION OF 2,2,4-TRIMETHYLPENTANE OVER MOLYBDENUM CATALYST

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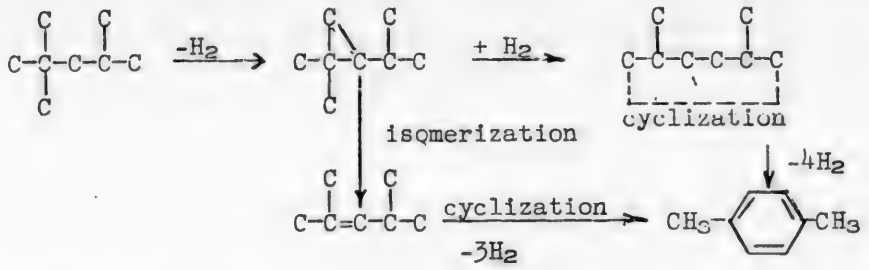
The smooth catalytic aromatization of the paraffin hydrocarbons depends on the presence in the ring of not less than six atoms of carbon. This makes possible the direct formation of a six-membered ring, the aromatization catalyst also contributing to the same result. However, a number of authors have shown that in the presence of the same aromatizing catalysts, aromatic hydrocarbons can also be formed in addition from alkanes which contain only 5 atoms of carbon in the longest chain, and which, without a radical change in their structure, are not capable of closing a six-membered ring. But in this case the reaction takes place with considerably lower yield, at a higher temperature, and is accompanied by cracking. Olefins with five atoms of carbon in their chain form aromatic hydrocarbons somewhat more readily than do paraffins [1].

2,2,4-Trimethylpentane (isooctane) is an example of the sort of structure which cannot directly form an aromatic ring.

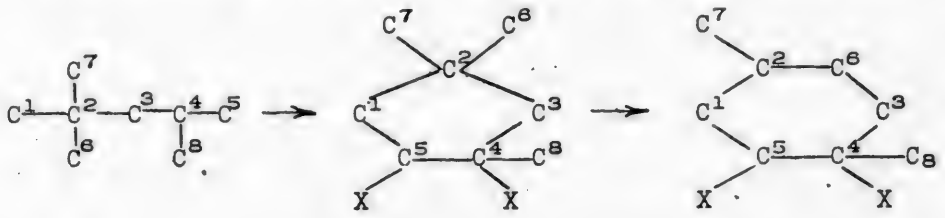
The aromatization of isooctane in the presence of chromium catalyst has been investigated by Hoog, Verheus, and Zuiderweg [2] at 460°, Marschner, Oblad, and Heard [3] at 480°, Green [4] at 480°, and Obolentsev and Usov [5] at 450, 480, and 510°. Green [4] aromatized 2 2,4-trimethylpentane in the presence of molybdenum catalyst at 550°. In most of the investigations, only the overall amount of aromatic hydrocarbons in the catalysate was determined. This did not favor an explanation of the mechanism of this reaction. The individual compositions of the aromatic hydrocarbons obtained were determined only in two investigations, and even in them, not completely. Green [4] observed in the catalysate obtained over molybdenum catalyst, a small amount of naphthalene, and in the mixture of xylenes he detected o-xylene. Obolentsev and Usov [5] found that the chief aromatic hydrocarbon formed from 2,2,4-trimethylpentane over chromium catalyst was p-xylene.

With regard to the possible mechanism of this reaction, there are three points of view which have been expressed in the literature concerning it. Green [4] explained the aromatization of 2,2,4-trimethylpentane by its preliminary isomerization into hydrocarbons which would permit direct cyclization with the formation of a six-membered ring. Obolentsev and Usov [5] assumed that this preliminary isomerization actually took place, and that it proceeded by means of a dehydrogenation step, with the formation of a three-membered ring: (see I, on following page). Herington and Rideal [6] assumed that aromatization took place by way of the formation of a five-membered ring, with its subsequent isomerization into a six-membered one, this isomerization proceeding in such a manner that the α-carbon of the side chain penetrated into a position neighboring

I



the C–C bond of the five membered ring. The penetration took place in that bond of the five-membered ring which was most distant from the closing bond:



Thus, in the case of 2,2,4-trimethylpentane, the penetration of the new carbon atom took place between carbon atoms 1 and 5, with the formation of p-xylene. If the penetration had taken place between carbon atoms 1 and 2, m-xylene would have been formed.

From what has been said above, it follows that in the case of mechanisms which predict the intermediate formation of three- and five-membered rings, the chief product of the aromatization of 2,2,4-trimethylpentane should be p-xylene. In accordance with both mechanisms, o-xylene cannot be formed.

It appeared to us that if the intermediate products of this reaction actually were alkanes isomeric with 2,2,4-trimethylpentane, or even cyclopentane hydrocarbons, it would be of interest to attempt to detect these hydrocarbons in the catalysate. Inasmuch as the catalytic aromatization of alkanes with six atoms of carbon in the chain takes place far from quantitatively, it seemed probable that the alkanes isomeric with 2,2,4-trimethylpentane, but having a chain of six carbon atoms, might, in case they were formed, be detected in the catalysate.

The experiments, carried out at 550° with molybdenum catalyst, showed that about 9 or 10% of p- and o-xylenes were formed, plus 2% of toluene, and small amounts of benzene and naphthalene. By means of the spectra of the combined scattering of light we detected a small amount of m-xylene. We did not succeed in detecting isomeric C_8 paraffins or cyclopentane hydrocarbons, either by the use of precise fractional distillation with effective columns, or by means of the spectra of the combined scattering of light. Thus, in contrast to the work of other authors, we showed that 2,2,4-trimethylpentane forms all three xylenes, the o- and p-xylenes in considerable amount, and the m-xylene in very small amount, and that in the catalysate it is impossible to detect either cyclopentane hydrocarbons or alkanes isomeric with the original 2,2,4-trimethylpentane. These facts, in particular the presence of o-xylene in the catalysate, cannot be completely explained either on the basis of the reaction mechanism which Herington and Rideal [6] proposed, in accordance with which the intermediate formation of cyclopentane hydrocarbons takes place, nor on the basis of the mechanism advanced by Obolentsev and Usov [5], in accordance with which there is the intermediate isomerization of the original alkane, taking place by way of a step involving the formation of a three-membered ring.

Most probably, isomerization is undergone not by the alkanes themselves, but by alkenes or semi-hydrogenated adsorption complexes, that is, the first stage of the reaction for the formation of xylene is neither isomerization nor demethylation, but dehydrogenation with the formation of 2,2,4-trimethylpentene-2 (which as is known, has a tendency to isomerize even at comparatively low temperatures), or with the formation of the corresponding semi-hydrogenated forms of isooctene. Thus, the dehydrogenation of the alkane into alkene in this case favors the further isomerization of the hydrocarbon. The absence of the isomers of 2,2,4-trimethylpentane in appreciable amounts even in the hydrogenated catalysate serves to indicate the fact that the velocity of the aromatization of the alkenes at the temperatures under investigation exceeds the velocity of isomerization or dehydrogenation.

On the other hand, the presence in the catalysate of toluene in an amount completely commensurate with the amount of xylenes formed, and the presence in the main fraction of catalysate of small amounts of 2,4-dimethylpentane, the high temperature at which the reaction of catalytic aromatization of paraffin hydrocarbons with five carbon atoms in the chain takes place, the large quantity of methane found by us in the gas, all these make it seem probable that in this case the process of aromatization of 2,2,4-trimethylpentane may approach the reaction of catalytic cracking, in which one of the initial factors, in this case, would be the breaking off of the methyl radical. The methyl group and the remaining radical (analogous to the semihydrogenated form) would have a tendency to stabilize themselves in the presence of hydrogen present on the surface, with the formation of the corresponding paraffins and olefins, or to react with each other with the formation of isomeric forms of octane, condensation products, and gaseous hydrocarbons. Under the conditions of the experiment, the isomeric forms of octane are easily aromatized with the formation of xylenes.

Inasmuch as the only isomeric heptane found in the catalysate was 2,4-dimethylpentane, it is necessary to assume that under the conditions of our experiments, the easiest thing of all was the breaking off (and consequently, the migration as well) of the methyl group attached to the fourth carbon atom.

The apparent energy of activation of the overall dehydrogenation reaction of 2,2,4-trimethyl pentane over molybdenum catalyst was shown to be 26,400 cal/mole, i.e., it was close to the energy of activation usually found [9] in the aromatization of paraffin hydrocarbons over oxide catalysts.

EXPERIMENTAL

The original hydrocarbons. Standard 2,2,4-trimethylpentane was distilled in a column with the effectiveness of 40 theoretical trays. Its properties were:

B.p. 99.6-99.7° at 760 mm; d_4^{20} 0.6908; n_D^{20} 1.3925.

MR_D found 39.39; computed for C_8H_{18} MR_D 39.14. Literature data [7]: b.p. 99.3° at 760 mm; d_4^{20} 0.6920; n_D^{20} 1.3915.

n-Heptane, also standard, had the following properties:

B.p. 98.3-98.4, at 760 mm; d_4^{20} 0.6834; n_D^{20} 1.3882; MR_D found 34.59; computed for C_7H_{16} MR_D 34.53. Literature data [8]: b.p. 98.38° at 760 mm; d_4^{20} 0.68378; n_D^{20} 1.38775.

The catalyst. We used molybdenum trioxide on aluminum oxide. The catalyst was prepared by Green's method [4] and contained 2% of molybdenum. A continuous layer of 65 ml of the catalyst was added to a quartz tube with inner diameter 14 mm.

Apparatus and method of work. The experiments were carried out in a circulating system by the method described previously [9]. All the experiments, except

for the experiments with different velocities of passage of the 2,2,4-trimethylpentane and experiments on the determination of the energy of activation, were carried out in a weak current of nitrogen (about 200 ml/hour) in order to decrease coke formation. In the determination of the amount and composition of the gas evolved, the amount of nitrogen passed through was taken into account. The catalysate was collected in a receiver with a stopcock and in a spiral boat cooled in a Dewar flask to -70°. The gas was collected in a gasometer, and in the experiments were accurate measurements of the gas volume was required during the course of the reaction, in a special gas-measuring device with a constant level of the sealing liquid. In the majority of experiments (except for the special experiments at different velocities) the volume velocity of passage was about 0.3. After the experiment, the catalyst was regenerated; air was passed through it at the temperature of the experiment for 8 hours, followed by 8 hours of reduction with hydrogen at the same temperature. Regeneration at 500° gave the same results as at 550°. With an increase in the number of regenerations, the initial activity of the catalyst fell somewhat, and the velocity of its poisoning increased.

Experiments with n-heptane. In order to check the activity of the catalyst, we set up comparison experiments on the aromatization of n-heptane. At 550° and a volume velocity of 0.3, the yield of catalysate after 5 hours, as determined every 30 minutes, rose from 43 to 65%. The average yield of catalysate over the 5 hours was 50.3%. The bromine number [10] was 7.0; this corresponded to about 4% of olefins. The index of refraction was 1.4571 after the first hour. For three hours it showed little change, and then fell to 1.4445 after 3.5 hours, and to 1.4367 after 4.5 hours. The amount of gas evolved amounted to 7 or 8 liters per hour.

At the same velocity of passage, but at 500°, the yield of catalysate was 74-76%, and its index of refraction was 1.4140 in the first hour and 1.4060 after 2.5 hours.

Analysis of the gas in the experiments with heptane: hydrogen about 90%, methane hydrocarbons about 7%, and olefins about 3%. At 550° and at 500°, the gas obtained had approximately the same composition.

Experiments with 2,2,4-trimethylpentane. In order to accumulate catalysate that might be studied, 18 experiments were carried out at 550°. Each experiment was carried out to the point where the index of refraction of the catalysate fell from 1.4200 - 1.4300 after the first hour to 1.4050 (for the original 2,2,4-trimethylpentane, n_D^{20} was 1.3925). Under these conditions, the duration of the experiments amounted to 4 or 5 hours during the work with fresh catalyst and 2 to 2.5 hours in the experiments with catalyst that had been repeatedly regenerated.

For the purpose of example, there are listed in Table 1 the results of three typical experiments on the aromatization of 2,2,4-trimethylpentane at 550 and 510°. As the poisoning of the catalyst progressed, the aromatic content of the catalysate decreased, the yield of catalysate increased, and the content of olefins in it decreased slightly (experiment 22).

Analysis of the gas showed that in contrast to n-pentane, 2,2,4-trimethylpentane formed a very appreciable amount of gaseous paraffin hydrocarbons, chiefly methane. At the same time, it was found that the composition of the gas depended little on whether or not the catalyst was active or already partially poisoned. The results of the gas analyses are listed in Table 2. (All the gas evolved during the experiment was analyzed).

In all, from the 18 experiments at 550°, 235 ml of catalysate was obtained (yield about 50%), containing about 5% of olefins. The catalysate was divided

into two parts, and underwent investigation by two different methods.

100 ml of the catalysate was fractionally distilled in a column capped by individual wire loops, with an effectiveness of 40 theoretical plates. The fractional distillation curve is shown in Fig. 1. 6 fractions were collected. After the determination of its bromine number, each fraction was hydrogenated in the cold in alcoholic solution with palladium-covered carbon. The residue from the distillation in the column was distilled with steam, dried, and distilled from a Wurtz flask. The terminal boiling point of the residue was 150°. The results of the fractional distillation, the properties, and the amounts of the different fractions, plus the indices of refraction of the fractions after hydrogenation are presented in Table 3.

TABLE 1

Expt. No. and Temp.	Time from start of expt., hours	Amount of 2,2,4-trimethylpentane passed through		Volume velocity	Liquid catalysate			Bromine number	Olefin content	Amount of gas in liters
		ml	g		Amount g	Amount %	n_D^{20}			
5 550°	1	19.0	13.1	0.29	4.4	33.6	1.4212	Not determined		4.0
	2	20.0	13.8	0.30	5.3	38.3	1.4154			3.5
	3	20.0	13.8	0.30	4.0	29.0	1.4286			4.0
	4	19.0	13.1	0.29	6.3	48.0	1.4105			3.5
	5	19.0	13.1	0.29	7.8	59.0	1.4032			3.0
11 550°	0.5	11.0	7.6	0.33	2.1	27.6	1.4330	Not determined		
	1	10.0	6.9	0.30	2.4	34.8	1.4265			
	1.5	10.0	6.9	0.30	3.3	47.8	1.4109			
	2	10.0	6.9	0.30	2.8	40.5	1.4078			
22 510°	1	16.1	11.1	0.24	4.0	40.0	1.4208	12.5	8.7	Not determined
	2	12.1	8.3	0.18	2.8	33.7	1.4456	11.8	8.3	
	3	16.0	11.0	0.24	4.7	42.7	1.4250	14.0	9.8	
	4	12.0	8.3	0.18	4.9	59.0	1.4056	16.8	11.8	

TABLE 2

Expt. No.	n_D^{20} 1 hour after start of experiment.	Composition of gas		
		H_2	C_nH_{2n+2}	C_nH_{2n}
4	1.4000	60.1	28.0	6.4
5	1.4212	59.0	33.0	5.7
6	1.4380	57.3	28.6	6.3

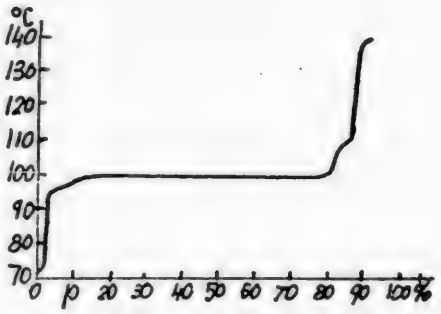


Fig. 1

Investigation of the different fractions permitted us to draw the following conclusions.

Fraction 1 consisted almost to the extent of half of olefins. Judging by

TABLE 3

Fraction No.	Boiling point in °	Percent by volume	Bromine No.	d_4^{20}	n_D^{20}	n_D^{20} after hydrogenation
Original catalysate	77.2-150	100	8.0	0.7285	1.4150	
I	77.2-97.7	7	46.0	0.7170	1.4068	1.3980
II	97.7-99.7	30	3.7	0.6959	1.3938	1.3930
III	99.7-99.7	42	12.2	0.6972	1.3950	1.3939
IV	99.7-110.5	6	3.8	0.6988	1.3952	1.3958
V	110.5-110.7	2	11.3	0.8415	1.4835	1.4795
VI	110.7-138.5	3.9	3.9	0.8591	1.4940	1.4932
VII residue..	138.5-150				1.5292	

the fractional distillation curve, the products of cracking, boiling below the original 2,2,4-trimethylpentane, were about 10%. After hydrogenation, benzene was detected in this fraction by the method of investigation using the spectra of combined light scattering.*

Judging from their physical properties, Fractions II and III were very close to the original 2,2,4-trimethylpentane.

Fraction IV was transitional.

Fraction V had a very high index of refraction, and therefore it was natural to suspect that it contained toluene. On the other hand, in it, and also in Fraction IV, there might have been homologs of cyclopentane or alkanes isomeric with the original 2,2,4-trimethylpentane, if aromatization had been preceded by isomerization and if part of the isomerized hydrocarbons had not undergone aromatization. Therefore, Fractions IV and V were passed through active silica gel, and a part was isolated which did not contain any aromatics and had the following characteristics: d_4^{20} 0.6916; n_D^{20} 1.3923. An investigation of the spectrum of combined light scattering of this non-aromatic portion showed that it consisted only of 2,2,4-trimethylpentane. Upon nitration [11] of the aromatic portion of Fraction IV and V (3 g) with fuming nitric acid (sp. gr. 1.5), dinitrotoluene was obtained (0.84 g). After a single recrystallization this had m.p. 67-68°. The toluene content of the catalysate amounted to about 2%.

Fraction VI must have contained a mixture of xylenes as the chief product of aromatization. In order to shed light on the composition of the xylenes, we used two methods: oxidation to phthalic acids, and nitration with fuming nitric acid.

Upon oxidation with potassium permanganate, by the method of Norris and Vaala [12] (0.3 ml), terephthalic and o-phthalic acids were obtained; no isophthalic acid was detected.

Upon nitration of Fraction VI, by the method of Reichel [13] (0.25 ml), 2,3,5-trinitro-p-xylene was obtained with m.p. 252° (according to the data in the literature, the m.p. is 254-255°), and in addition, there were obtained oily nitroproducts which indicated that o-xylene had been present in the original mixture. No products of the nitration of m-xylene were detected (the crystals of nitrated products obtained were completely soluble in acetone). However, according to the spectrum of the combined scattering of light, this fraction did contain m-xylene, although in very insignificant quantity. The approximate content of the o- and p-xylenes in the catalysate was 9 or 10%.

* We wish to take the occasion to express our profound appreciation to M. I. Butuev for investigating the spectra of the combined scattering of light for the fractions.

Fraction VII (residue) was treated with picric acid. A small amount of crystals precipitated with m.p. (without recrystallization) of 147°. This corresponded to the m.p. of naphthalene picrate.

The second portion of the catalysate (135 ml) was investigated by a different method. By means of fractional distillation of the catalysate from a flask with a dephlegmator, it was divided into two fractions:

I. 40-132°. 89 g; n_D^{20} 1.4040; bromine number 9.1; olefins 5.4%.

II. 132-140°; 2 g; n_D^{20} 1.4960.

III. Residue; n_D^{20} 1.5186 after steam distillation.

Fraction I was hydrogenated in the cold with palladium-covered carbon. The hydrogenation took place with difficulty, despite the addition of a catalyst during the experiment. Instead of the computed 1.25 liters of hydrogen, 1.1 liter was absorbed. After hydrogenation, the catalysate had the following properties: d_4^{20} 0.7110; n_D^{20} 1.4035. The aromatic hydrocarbons and the traces of unsaturateds were removed by treatment with Katvinkel's mixture, 17% being absorbed. The catalysate freed from aromatics had the following properties: d_4^{20} 0.6952; n_D^{20} 1.3930, and was distilled in a column. The fractional distillation curve is seen in Fig. 2.

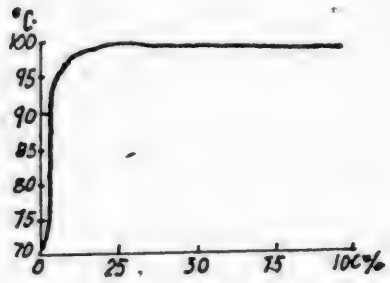


Fig. 2.

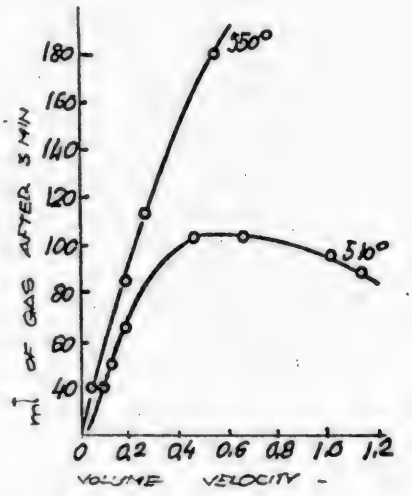


Fig. 3.

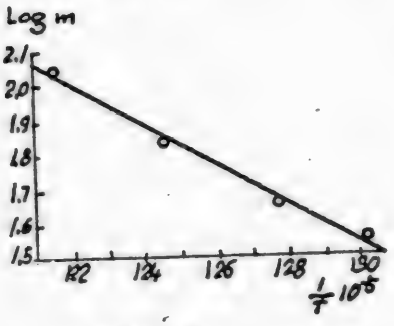


Fig. 4.

TABLE 4

Expt. No.	Volume velocity	n_D^{20}	Bromine number
231	0.42	1.4068	3.0
232	0.63	1.4050	2.2
233	0.12	1.4211	2.5
234	0.87	1.3985	4.0
235	0.42	1.3968	

In the chief fraction (10%), with boiling range 71-98°, after a supplementary purification from traces of benzene by filtration through 10 ml of active silica gel, a small amount of 2,4-dimethylpentane was detected (by means of the frequency 809 (65) cm^{-1}). The main portion of the catalysate freed from aromatics

had n_D^{20} 1.3938, and judging [illegible] of the combined scattering of light corresponded to pure 2,2,4-trimethylpentane.

The experiments arranged for different velocities of passage of the original hydrocarbon at 510° showed (cf. Table 4 and Fig. 3) that in contrast to the experiments with n-pentane in the presence of vanadium catalyst, in the case of 2,2,4-trimethylpentane with a molybdenum catalyst, there was no constant evolution of gas when there was a change in the velocity of passage of the hydrocarbon. At 510°, as the velocity of passage increased, the curve for the evolution of gas passed through a maximum, corresponding to a volume velocity of about 0.6. At 550°, it was impossible to attain this maximum up to a volume velocity of 0.5. Thus, under the conditions of the latter experiment with 2,2,4-trimethylpentane, we still did not have complete saturation of the surface of the catalyst with the hydrocarbon.

TABLE 5

Expt. No.	Temperature, (°)	n_D^{20}	Bromine number	Clefin content, %	Gas evolved in ml after 3 min
1	510	1.4130	9.3	6.5	64.7
2	490	1.4034	8.0	5.6	35.1
3	530	1.4120	8.0	5.6	69.7
4	510	1.4050	6.0	4.2	46.2
5	550	1.4144	2.1	1.5	109.3

The experiments arranged for different temperatures and volume velocity of 0.3 gave the following results (Table 5).

Experiment 1, as usual [9], departed from the general rules. The other results obtained satisfied Arrhenius' equation, giving an apparent energy of activation of the overall dehydrogenation reaction of 2,2,4-trimethylpentane equal to 26,400 cal/mole (Fig. 4).

We express our profound thanks to Academician B.A.Kazansky for his unflagging interest in this work and for a number of valuable suggestions.

SUMMARY

1. The aromatization of 2,2,4-trimethylpentane (isooctane) has been investigated over molybdenum catalyst in the temperature interval 490-550° and within the limits of volume velocity of 0.1 to 0.9.

2. At 550° and a volume velocity of 0.3, the yield of liquid catalysate amounted to 30-50%, and the gas evolved contained 60% of hydrogen and 30% of methane.

3. We were unable to detect in the catalysate alkanes isomeric with the original 2,2,4-trimethylpentane, or cyclopentane hydrocarbons, either by means of fractional distillation of the catalysate with effective columns or by means of an investigation of the spectra of the combined scattering of light of the different fractions.

4. At 550° and a volume velocity of 0.3, the products of the aromatization of 2,2,4-trimethylpentane in the presence of molybdenum catalyst were: o- and p-xylenes (9-10%), toluene (2%), as well as benzene, naphthalene, and m-xylene (in small amounts). Of products of lower molecular weight, it was possible to detect, by means of the spectra of combined scattering of light, only a small amount of 2,4-dimethylpentane.

5. Inasmuch as the formation of these products is not explained by either of the previously proposed mechanisms of reaction, new considerations on the course of this reaction are expressed.

6. The apparent energy of activation of the overall reaction for the dehydrogenation of 2,2,4-trimethylpentane equaled 26,400 cal/mole.

7. Under the conditions of investigation, with the volume velocities and the temperatures used, saturation of the surface of the catalyst with the original hydrocarbon was not attained.

LITERATURE CITED

[1] H.S.Taylor, J.Turkevich, Trans. Faraday Soc., 35, 921 (1939).

[2] H.Hoog, J.Verheus, F.Zuiderweg, Trans. Faraday Soc., 35, 993 (1939).

[3] A.G.Oblad, R.F.Marschner, L.Heard, J.Am.Chem.Soc., 62, 2066 (1940).

[4] G.Green, J.Inst.Petroleum, 28, 179 (1942).

[5] R.D.Obolentsev and Yu. N.Usov, J.Gen.Chem. 16, 933 (1946).

[6] E.F.G.Herington, E.K.Rideal, Proc. Royal Soc., 184, No. 999, 434, 447 (145).

[7] G. Calingaert, T.A.G.Edgar, J.Am.Chem.Soc. 51, 1546 (1926).

[8] A.F.Shepard, A.L.Henne, T.Midgely, Jr., J.Am.Chem.Soc. 53, 1948 (1931).

[9] A.F.Plate and G.A.Tarasova, J.Gen.Chem. 13, 21 (1943).

[10] G.D.Galpern and Vinogradova, Chemistry of Solid Fuels, 8, 384 (1937).

[11] F.Beilstein, A.Kuhlberg, Ann., 155, 13 (1870).

[12] J.F.Norris, G.T.Vaala, J.Am.Chem.Soc., 61, 2131 (1939).

[13] H.P.Reichel, Chem. Ztg., 55, 744 (1931); Chem. Abs. 25, 5876 (1931).

[14] E.H.Huntress, S.P.Muliken. Identification of Pure Organic Compounds. Wiley and Sons. N.Y., 1941, p. 507.

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THE PREPARATION OF SULFAMIDE

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An investigation of the properties and reactions of the complete amide of sulfuric acid, or sulfamide, is of great scientific interest. A very great number of communications have been printed on the preparation of sulfamide [1], but in these communications either the synthesis has not been described with sufficient precision, or the synthesis required original materials which were difficult of access, or else the synthesis was carried out under conditions difficult to produce in the average laboratory.

For the industrial production of sulfamide there is a very good method, namely, the action of ammonia on sulfuryl fluoride [2]. For the production of sulfuryl fluoride on an industrial scale we now have satisfactory methods, and there is no doubt that still better methods may yet be developed without special difficulty. But the preparation and use of sulfuryl fluoride in laboratories, in small amounts, with only the objective of the synthesis of sulfamide, is of course very difficult. There is also a second method for the production of sulfamide, namely, the action of sulfuryl chloride on a mixture of liquid ammonia with any appropriate solvent at a temperature of the order of 60°, with vigorous stirring. It has been shown [3] that in this manner sulfamide may be obtained in a yield 86% of the theoretical. This method, like the preceding one, is little suited for the preparation of comparatively small amounts of sulfamide in ordinary laboratories, as it requires special expensive apparatus, which it scarcely pays to buy for the preparation of small amounts of sulfamide.

In order to make it possible for all who wish to investigate the properties and reactions of sulfamide or to use it for preparative purposes to do so, there is given below a detailed description of the synthesis of sulfamide. This method of synthesis is based on a reaction first used by Regnault for the preparation of sulfamide, and differs from those described in the literature, in the first place, in a number of details, and in the second by the precision of the description, which will permit any chemist-experimenter to reproduce it accurately, and to obtain the yields indicated. The conditions of synthesis are entirely accessible to any laboratory.

According to the old data in the literature, the yields of sulfamide from sulfuryl chloride and ammonia were not high, and in the best case reached 15-20% of theory. According to a recent communication [3], when very low temperatures are used, the yields reach 86%; this, however, has not been checked and verified. In the method described below, the yield amounts to 44% of theory, and this can be considered completely satisfactory, as the starting materials are inexpensive and easily obtained.

EXPERIMENTAL

The work was carried out in an effective hood. An eight-liter wide-necked jar was supported firmly in a large bath*, and inside the jar there were placed

* The bath must be of fairly large dimensions in order that the used up cooling mixture may be conveniently removed from it and new cooling mixture added. This, depending on the size of the bath must be done every 15 to 45 minutes.

a powerful propellor stirrer, a thermometer, and a gas-inlet tube, of 10-12 mm diameter, leading almost to the bottom of the jar. Into the jar there was poured 3 liters of dry carbon tetrachloride*, and the bath was filled with a cooling mixture carefully prepared from crushed ice and salt and set in motion with a stirrer. When the temperature of the carbon tetrachloride was lowered to -8°, a strong current of ammonia** was passed through the gas-inlet tube, and a mixture of 500 ml of sulfuryl chloride*** and 2500 ml of dry carbon tetrachloride was added in 10-50 ml portions. Each addition resulted in a sharp rise in temperature, and was accompanied by the appearance of a thick mist. The amount of mixture added each time had to be such that the temperature did not rise to more than -2°. After each addition, there was a pause until the temperature of the mixture had fallen to -8°. During the very first addition, a flocculent, colorless precipitate formed. This gradually collected in large lumps. When these lumps began to hinder the operation of the stirrer, they were removed from the reaction mixture by means of a porcelain boat and collected in a 4 to 5 liter enameled pot. It was usually necessary to remove these lumps 2 or 3 times, after the addition of a quarter, a half, and three-quarters of the entire amount of sulfuryl chloride. Under unusual conditions, the precipitate did not collect in lumps and remained dispersed until the end of the process. The character of the precipitate did not affect the yield of sulfamide. It is necessary to emphasize that a rapid current of ammonia was passing through all the time. If no cloud was formed during the addition of the next portion of sulfuryl chloride, or if a small cloud was formed, this meant that the current of ammonia was not sufficient, and it had to be increased. When the temperature in the cooling bath rose to -15°, it had to be changed for a fresh mixture. The entire process usually took 10 to 15 hours, and required the work of two men, as a fairly frequent change of the cooling mixture was necessary. The addition of sulfuryl chloride could be discontinued at night and resumed on the following day without diminishing the yield of sulfamide. After all the sulfuryl chloride had been added, the passage of ammonia was continued for an additional 30 minutes, and 3 liters of water was then added and stirred, until all the precipitate had gone into solution.**** The aqueous solution was separated from the carbon tetrachloride and mixed with the previously removed lumps of reaction product which were in the enameled pot. The mixture was stirred by hand until all the precipitate had gone into solution, and then the solution was boiled vigorously in the open pot, under a hood, until a thermometer dipped into the liquid indicated 108-109°. During the boiling, a fairly large amount of ammonia was evolved. The final volume of the liquid was about 2.5 liters.

The solution was allowed to stand at room temperature for 12 to 15 hours, and was then filtered with suction of a Buchner funnel of 150 mm diameter to

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*Technical carbon tetrachloride was dried with calcium chloride and distilled. The first fraction was discarded, the distillate coming over within the limits 76-78° being collected.

**The ammonia from a cylinder was dried in a column filled with powdered caustic potash.

***The sulfuryl chloride used was prepared by the dismutation of chlorosulfonic acid in the presence of metallic mercury, with boiling, and repeated distillation within the limits 68-72°. The same results were obtained with commercial sulfuryl chloride which was distilled without a dephlegmator, the fraction boiling within the limits 67-72° being collected.

****The carbon tetrachloride was carefully separated from the aqueous solution, dried with calcium chloride and distilled. It could then be used in another preparation of sulfamide.

remove precipitated ammonium chloride. The precipitate was carefully pressed out and washed 3 times with 50 ml portions of ice water. After drying in the air, the weight of the precipitate was about 335 g. The combined filtrates were evaporated in a round-bottomed 3-liter flask in vacuum on a water bath heated to 60-70°. After 650 ml of water had distilled off, the precipitated ammonium chloride was filtered with suction and washed 3 times with 50 ml portions of ice water.* After drying in the air, the weight of the precipitate was about 150 g. The combined filtrates were evaporated a second time in vacuum on a water bath heated to 60-70°. After 650 ml had distilled off, the precipitated ammonium chloride was again filtered with suction and washed 3 times with 50 ml portions of ice water. After drying in the air, the weight of the precipitate was about 150 g. The combined filtrates were evaporated in vacuum on the boiling water bath until there was no further distillation, a distillate of about 300 ml being thus collected. The residue in the flask was a thick, viscous mass, containing a small amount of crystals. To the residue in the flask there was added 1 liter of boiling 0.5 N hydrochloric acid. The mixture was vigorously shaken until everything went into solution, and the solution was boiled with a reflux condenser for 15 minutes,** the temperature of the liquid during this process being 106-107°. During the boiling, the liquid became cloudy with precipitated sulfur and a small amount of sulfur dioxide was evolved. After 15 minutes of boiling the liquid was cooled with running water, filtered through a crinkled filter, and neutralized with 20% ammonia until there was a neutral reaction to Congo red. The solution obtained was concentrated in vacuum on a boiling water bath until about 950 ml of water had distilled off. The precipitated ammonium chloride was filtered off with suction and washed 3 times with 25 ml portions of ice water. After drying in the air, the weight of precipitate was about 100 g. Thus, the total amount of ammonium chloride obtained was about 635 g.***

The combined filtrates were evaporated in vacuum on a boiling water bath, until all the water had been distilled off. Usually about 150 ml of water came off, and then the residue in the flask was in the form of a thick, viscous, transparent mass. To this still hot product, 1 liter of acetone was added,**** and the mixture was very vigorously shaken. After several minutes, the semiliquid product hardened completely***** in the form of fine little lumps. The cooled solution of sulfamide in acetone was poured off from the precipitate, the precipitate was transferred to a mortar and carefully ground, and again transferred to the same flask and 1 liter of acetone was added. The flask was connected to a reflux condenser and the mixture was boiled on a water bath with continual

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* It is possible to distill off about 1300 ml of water at once, but then the evaporation is accompanied by very violent bumping. It is safer and quicker to evaporate twice in vacuum, and to filter off the ammonium chloride with suction twice.

** Longer boiling decreases the yield of sulfamide. Shorter boiling requires repeated acid hydrolysis, which considerably complicates the work, and does not increase the yield. Therefore it is necessary to add to the concentrated residue boiling 0.5 N acid, and to heat the solution quickly to the boiling point, in order to decrease the influence of the period "before the beginning of the boiling".

*** The ammonium chloride need not be dried and weighed, since this does not increase the yield of sulfamide. However a control of the amount of ammonium chloride is useful, especially when this reaction is carried out for the first time, as this controls confirms the correctness of the method of carrying out the entire process.

**** Technical acetone was dried with calcium chloride and distilled twice the 55-58° fraction being collected.

***** It is necessary to shake the mixture vigorously until it hardens completely. During this process, the precipitate assumes the form of fine lumps, which are easily removed from the flask. The fine layer on the walls of the flask is also easily removed. If the mixture is not stirred, or is stirred with insufficient vigor, the liquid precipitate hardens into a continuous mass or into large lumps, which are very difficult to remove from the flask.

shaking by hand for 10 to 15 minutes. After cooling, the acetone solution was poured off. Still another 1 liter of acetone was added* and boiled for another 15 minutes. After cooling, the acetone solution was filtered with suction on a Buchner funnel of 200 mm diameter, the precipitate was carefully pressed out, again transferred to a flask, boiled with 500 ml of acetone, cooled, and filtered with suction. It was again transferred to the flask, 500 ml of acetone added, again boiled, and after cooling, the precipitate filtered with suction and pressed. After this the precipitate was discarded.** Thus, a total of 5 extractions with acetone was carried out. This ensured the completeness of extraction of the sulfamide. It is recommended that each acetone extract be concentrated separately, in order to have the possibility of judging how successfully the extraction has been carried out. The first acetone extract was filtered, placed in a weighed one and a half liter conical flask, and the acetone completely driven off on the water bath, which, toward the end of the distillation, was brought to the boiling point. The same thing was done with the second, third, fourth, and fifth extracts. The residue from the distillation*** upon cooling quickly crystallized completely to give a characteristic, radial crystalline mass. Usually the first extract gave about 120 g of sulfamide, the second about 65 g, the third about 50 g, the fourth about 30 g, and the fifth about 6 g; a total of about 270 g of crude sulfamide was obtained. Sometimes, with very careful grinding, it is possible to remove the sulfamide in 4 extractions, and sometimes it is necessary to make 6 extractions. The extraction should be stopped after the amount of sulfamide extracted is less than 10 g.

The sulfamide thus obtained is in the form of large ray-shaped crystals, colored a light yellow by impurities.

For purification, all the sulfamide obtained (about 270 g) was crystallized from 600 ml of boiling ethyl alcohol (96°). Upon cooling, large, heavy, colorless crystals precipitated. They were filtered with suction and washed 3 times with cold alcohol. After drying in the air, 215 g of large snow-white crystals of sulfamide were obtained, with m.p. 92-93°. The mother liquor and the wash liquid were concentrated in vacuum to a volume of 150 ml, 2 g of activated carbon was added, the mixture was boiled for 2 or 3 minutes, and then filtered. Upon cooling, sulfamide precipitated. This was filtered off with suction and washed 3 times with 5 ml portions of alcohol. Thus, an additional approximately 22 g of sulfamide of the same quality was obtained.

The mother liquor was evaporated to dryness in vacuum, the residue extracted with 200 ml of acetone, the solution filtered, and the acetone driven off. In the residue there was obtained about 20 g of crude sulfamide, which was treated with the next portions of sulfamide or crystallized from ethyl acetate. The total yield of pure sulfamide was 235-240 g, and of crude about 20 g, i.e., together there was about 260 g, or 44% of the theoretical. In order to obtain a purer preparation, with m.p. 91.5-92°, the sulfamide was recrystallized a second time from alcohol. For 100 g of sulfamide it was convenient to take 250 ml of boiling alcohol. The yield was 80-85 g. If the alcoholic mother liquids were evaporated in vacuum, then the loss upon repeated crystallization was negligible.

SUMMARY

A method for the preparation of sulfamide from sulfuryl chloride and ammonia with a yield of about 44% of theory has been described in detail.

LITERATURE CITED

[1] Regnault, Ann. chim. phys., (2) 69, 170 (1838); Traube, Ber., 25, 2472 (1892); 26, 607 (1893); Ruff, Ber., 36, 2900 (1903), Ephraim and Michel, Ber., 42, 3833 (1909); Ephraim and Gurevich, Ber., 43, 138 (1910); Battegai and Denivel,

See following page.

Comptes rend., 194, 2216 (1932); Bull., (4) 53, 1242 (1933); Oswald, U.S.Patent 2,117,628 (1938); Chem. Abs., 32, 5165 (1938).

[2] Traube and Rebke, Ber., 56, 1656 (1923); Shroyer, Thesis University of Chicago, 1928, cited by Audris; Chem. Rev., 26, 49 (1940); Bud and Batti, J. Soc. Chem. Ind., 52, 2, 346 T (1933).

[3] Degering and Gross, Ind. Eng. Chem. 35, 751 (1943); U.S.Patent 2,407,481; Chem. Abs., 1946, 7538; see also Anderson and Miller, Chem. Abs., 1948, 8102; J. Am. Pharm. Assn., Sci. Ed. 37, 204 (1948).

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• It is not necessary to use fresh acetone each time. While the second extraction is being carried out, the acetone from the first extraction is simultaneously being distilled off, and the distillate can be used for the third extraction etc.

•• The dry residue from the extraction with acetone weighs about 450 g and consists chiefly of ammonium chloride and ammonium sulfaminate. From this precipitate it is possible to obtain, by repeated hydrolysis with 0.5 N hydrochloric acid, only about 3.0 g of sulfamide, which of course is not worth considering.

••• A transparent, light yellow liquid.